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OM protein - protein search, using sw model

Run on: July 26, 2004, 12:38:32 ; Search time 49.3333 Seconds  
(without alignments)  
3991.938 Million cell updates/sec

Title: US-09-806-194A-18  
Perfect score: 3651  
Sequence: 1 MLPGLALLLLAAWTARALEV.....QQNGYENPTYKFFEQMQNKK 697

Scoring table: BLOSUM62  
Gapop 10.0 , Gapext 0.5

Searched: 1586107 seqs, 282547505 residues

Total number of hits satisfying chosen parameters: 1586107

Minimum DB seq length: 0  
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%  
Maximum Match 100%  
Listing first 45 summaries

Database : A\_Geneseq\_29Jan04:\*  
1: geneseqp1980s:\*  
2: geneseqp1990s:\*  
3: geneseqp2000s:\*  
4: geneseqp2001s:\*  
5: geneseqp2002s:\*  
6: geneseqp2003as:\*  
7: geneseqp2003bs:\*  
8: geneseqp2004s:\*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	Query		DB	ID	Description
		Match	Length			
1	3651	100.0	697	3	AAy88429	Aay88429 Human APP
2	3651	100.0	697	4	AAU07209	Aau07209 Human bet
3	3651	100.0	697	4	AAE10636	Aae10636 Human amy
4	3651	100.0	697	4	AAE06866	Aae06866 Human amy
5	3651	100.0	697	4	AAE02588	Aae02588 Human amy
6	3651	100.0	697	4	AAU06610	Aau06610 Human Amy
7	3651	100.0	697	5	ABB78597	Abb78597 Human APP
8	3643	99.8	697	3	AAy88428	Aay88428 Human APP
9	3643	99.8	697	4	AAU07208	Aau07208 Human bet

10	3643	99.8	697	4	AAE10635	Aae10635	Human	amy
11	3643	99.8	697	4	AAE06865	Aae06865	Human	amy
12	3643	99.8	697	4	AAE02587	Aae02587	Human	amy
13	3643	99.8	697	4	AAU06609	Aau06609	Human	Amy
14	3643	99.8	697	5	ABB78596	Abb78596	Human	APP
15	3641	99.7	695	3	AAAY88435	Aay88435	Human	APP
16	3641	99.7	695	4	AAU07206	Aau07206	Human	bet
17	3641	99.7	695	4	AAE10633	Aae10633	Human	amy
18	3641	99.7	695	4	AAE06863	Aae06863	Human	amy
19	3641	99.7	695	4	AAE02585	Aae02585	Human	amy
20	3641	99.7	695	4	AAU06607	Aau06607	Human	Amy
21	3641	99.7	695	5	ABB78594	Abb78594	Human	APP
22	3641	99.7	695	7	ADB87313	Adb87313	Human	amy
23	3638	99.6	697	3	AAAY88430	Aay88430	Human	APP
24	3638	99.6	697	4	AAU07210	Aau07210	Human	bet
25	3638	99.6	697	4	AAE10637	Aae10637	Human	amy
26	3638	99.6	697	4	AAE06867	Aae06867	Human	amy
27	3638	99.6	697	4	AAE02589	Aae02589	Human	amy
28	3638	99.6	697	4	AAU06611	Aau06611	Human	Amy
29	3638	99.6	697	5	ABB78598	Abb78598	Human	APP
30	3638	99.6	740	7	ADB87314	Adb87314	Human	amy
31	3638	99.6	740	7	ADB87312	Adb87312	Human	amy
32	3636	99.6	695	2	AAW19490	Aaw19490	APP695	mu
33	3636	99.6	695	2	AAW19504	Aaw19504	APP695	mu
34	3633	99.5	695	1	AAP81692	Aap81692	Sequence	
35	3633	99.5	695	2	AAR26338	Aar26338	APP695.	3
36	3633	99.5	695	2	AAAY20233	Aay20233	Human	bet
37	3633	99.5	695	2	AAAY07221	Aay07221	Amyloid	p
38	3633	99.5	695	3	AAAY88434	Aay88434	Human	APP
39	3633	99.5	695	3	AAAY44705	Aay44705	Human	bet
40	3633	99.5	695	4	AAE10632	Aae10632	Human	wil
41	3633	99.5	695	4	AAE06862	Aae06862	Human	wil
42	3633	99.5	695	4	AAE02584	Aae02584	Human	amy
43	3633	99.5	695	4	AAU06606	Aau06606	Human	Amy
44	3633	99.5	695	5	ABB78593	Abb78593	Human	APP
45	3633	99.5	695	5	AAG68315	Aag68315	Human	amy

# ALIGNMENTS

## RESULT 1

AAAY88429

ID AAY88429 standard; protein; 697 AA.

XX

AC AAY88429;

XX

DT 03-AUG-2000 (first entry)

XX

DE Human APPSW-KK amino acid sequence.

XX

KW Aspartyl protease; aspartase; amyloid precursor protein; APP; Asp 2;

KW Alzheimer's disease; beta secretase site; APPSW-KK.

XX

OS Homo sapiens.

XX

PN WO200017369-A2.



Qy	181	GVEFVCCPLAEESDNVDSADAEEDDSDVVWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDDSDVVWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDEDGDEVEEEAEEPVEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDEDGDEVEEEAEEPVEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEI SEVNLD AEF	600
Db	541	DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEI SEVNLD AEF	600
Qy	601	RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITL VMLKKKQYTSIHHGV	660
Db	601	RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITL VMLKKKQYTSIHHGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK	697
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK	697

# RESULT 2

AAU07209

ID AAU07209 standard; protein; 697 AA.

XX

AC AAU07209;

XX

DT 24-OCT-2001 (first entry)

XX

DE Human beta-amyloid protein precursor, APP695-Sw-KK.

XX

KW Human; aspartyl protease 1; Asp-1; nootropic; neuroprotective;

KW aspartyl protease 2; Asp2; amyloid protein precursor; APP;

KW beta-secretase; Alzheimer's disease; APP695-Sw-KK.

XX

OS Homo sapiens.

XX

FH Key Location/Qualifiers

FT Misc-difference 595

FT /note= "Wild type Lys substituted by Asn"

FT Misc-difference 596



FT /note= "Wild type Met substituted by Leu"  
 XX  
 PN WO200149097-A2.  
 XX  
 PD 12-JUL-2001.  
 XX  
 PF 09-MAY-2001; 2001WO-IB000797.  
 XX  
 PR 09-MAY-2001; 2001WO-IB000797.  
 XX  
 PA (BIEN/) BIENKOWSKI M J.  
 PA (GURN/) GURNEY M E.  
 PA (HEIN/) HEINRIKSON R L.  
 PA (PARO/) PARODI L A.  
 PA (YANR/) YAN R.  
 XX  
 PI Bienkowski MJ, Gurney ME, Heinrikson RL, Parodi LA, Yan R;  
 XX  
 DR WPI; 2001-502548/55.  
 DR N-PSDB; AAS11709.  
 XX  
 PT Novel purified polypeptide comprising fragment of mammalian aspartyl  
 PT protease 2, lacking Asp2 transmembrane domain and retaining beta  
 PT secretase activity of Asp2 useful for identifying inhibitors of Asp2  
 PT activity.  
 XX  
 PS Example 6; Page 147-149; 185pp; English.  
 XX  
 CC The invention relates to a novel purified polypeptide comprising a  
 CC fragment of mammalian aspartyl protease 2 (Asp2) protein which lacks the  
 CC Asp2 transmembrane domain and the Asp2 protein, and where the polypeptide  
 CC and the fragment retain the beta-secretase activity of the mammalian Asp2  
 CC protein. Also included is an isoform of amyloid protein precursor (APP)  
 CC comprising the amino acid sequence of a APP or its fragment containing an  
 CC APP cleavage site recognisable by a mammalian beta-secretase, and further  
 CC comprising two lysine residues at the carboxyl terminus of the amino acid  
 CC sequence of the mammalian APP or APP fragment. The polypeptides are used  
 CC for assaying for modulators of beta-secretase activity; identifying  
 CC agents that inhibit the APP processing activity of human Asp2 aspartyl  
 CC protease (Hu-Asp2); identifying agents that modulate the activity of Asp2  
 CC ; and for reducing cellular production of amyloid beta (Abeta) from APP.  
 CC Agents identified by the above methods are useful for treating  
 CC Alzheimer's disease; and for identifying modulators of amyloid-beta  
 CC (Abeta) peptide production, for use in designing therapeutics for the  
 CC treatment or prevention of Alzheimer's disease. Probes and primers  
 CC derived from Asp nucleic acid sequences are useful for detecting Hu-Asp  
 CC nucleic acids in in vitro assays and in Northern and Southern blots. The  
 CC present sequence represents the amino acid sequence of human amyloid  
 CC protein precursor, APP695-Sw-KK, used in the method of the invention  
 XX  
 SQ Sequence 697 AA;  
  
 Query Match 100.0%; Score 3651; DB 4; Length 697;  
 Best Local Similarity 100.0%; Pred. No. 5.1e-253;  
 Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLDAAF	600
Db	541	DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLDAAF	600
Qy	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMKLLKKQYTSIHHGV	660
Db	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMKLLKKQYTSIHHGV	660
Qy	661	VEVDAAVTPEERHLSKMQONGYENPTYKFFEQMKNKK	697
Db	661	VEVDAAVTPEERHLSKMQONGYENPTYKFFEQMKNKK	697

RESULT 3

AAE10636

ID AAE10636 standard; protein; 697 AA.

XX

AC AAE10636;

XX

DT 10-DEC-2001 (first entry)

XX

DE Human amyloid protein precursor 695-Sw-KK (APP695-Sw-KK) isoform.

XX  
 KW Human; aspartyl protease 1; Aspl; amyloid precursor protein;  
 KW Alzheimer's disease; AD; dementia; neurofibrillary tangle; gliosis;  
 KW amyloid plaque; neuronal loss; proteolytic; nootropic; neuroprotective;  
 KW APP695-Sw-KK; mutant; mutein.  
 XX  
 OS Homo sapiens.  
 OS Synthetic.  
 XX  
 FH Key Location/Qualifiers  
 FT Misc-difference 595  
 FT /note= "Wild-type Lys substituted with Asn"  
 FT Misc-difference 596  
 FT /note= "Wild-type Met substituted with Leu"  
 XX  
 PN GB2357767-A.  
 XX  
 PD 04-JUL-2001.  
 XX  
 PF 22-SEP-2000; 2000GB-00023315.  
 XX  
 PR 23-SEP-1999; 99US-00404133.  
 PR 23-SEP-1999; 99US-0155493P.  
 PR 23-SEP-1999; 99WO-US020881.  
 PR 13-OCT-1999; 99US-00416901.  
 PR 06-DEC-1999; 99US-0169232P.  
 XX  
 PA (PHAA ) PHARMACIA & UPJOHN CO.  
 XX  
 PI Bienkowski MJ, Gurney M;  
 XX  
 DR WPI; 2001-444208/48.  
 DR N-PSDB; AAD17872.  
 XX  
 PT Polypeptide comprising fragments of human aspartyl protease with amyloid  
 PT precursor protein processing activity and alpha-secretase activity, for  
 PT identifying modulators useful in treating Alzheimer's disease.  
 XX  
 PS Example 6; Page 117-119; 187pp; English.  
 XX  
 CC The patent discloses human aspartyl protease 1 (hu-Aspl) or modified Aspl  
 CC proteins which lack transmembrane domain or amino terminal domain or  
 CC cytoplasmic domain and retains alpha-secretase activity and amyloid  
 CC protein precursor (APP) processing activity. The proteins of the  
 CC invention are useful for assaying hu-Aspl alpha-secretase activity, which  
 CC in turn is useful for identifying modulators of hu-Aspl alpha-secretase  
 CC activity, where modulators that increase hu-Aspl alpha-secretase activity  
 CC are useful for treating Alzheimer's disease (AD) which causes progressive  
 CC dementia with consequent formation of amyloid plaques, neurofibrillary  
 CC tangles, gliosis and neuronal loss. Hu-Aspl protease substrate is useful  
 CC for assaying hu-Aspl proteolytic activity, by contacting hu-Aspl protein  
 CC with the substrate under acidic conditions and determining the level of  
 CC hu-Aspl proteolytic activity. The present sequence is human amyloid  
 CC protein precursor 695-Sw-KK (APP695-Sw-KK) isoform which is obtained by  
 CC the addition of two lysine residues (KK motif) at the C-terminal of  
 CC App695-Sw isoform which is generated by the Swedish mutation APP695,  
 CC where Lys at position 595 is replaced with Asn and Met at position 596 is

CC replaced with Leu. APP695-Sw-KK isoform is useful for assaying the beta-  
CC secretase activity of human aspartyl protease 2a (hu-Asp2a) protein  
XX  
SQ Sequence 697 AA;

Query Match 100.0%; Score 3651; DB 4; Length 697;  
Best Local Similarity 100.0%; Pred. No. 5.1e-253;  
Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG 120
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360

Qy    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480

Qy    481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTLTETKTTVELLPVNGEFSL 540
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTLTETKTTVELLPVNGEFSL 540

Qy    541 DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    541 DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600

Qy    601 RHDSGYEVHHQKL VFFAEDVGSNKGAI IGLMVGGVVIATVIVITL VMLKKKQYTSI HHGV 660
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    601 RHDSGYEVHHQKL VFFAEDVGSNKGAI IGLMVGGVVIATVIVITL VMLKKKQYTSI HHGV 660

Qy    661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697
```

RESULT 4

AAE06866

ID AAE06866 standard; protein; 697 AA.

XX

AC AAE06866;

XX

DT 23-OCT-2001 (first entry)

XX

DE Human amyloid precursor protein 695-Sw-KK (APP695-Sw-KK) isoform.

XX

KW Human; aspartyl protease; Asp; beta-amyloid precursor protein 695-Sw-KK;

KW beta-secretase; Alzheimer's disease; dementia; amyloid plaque; gliosis;

KW neurofibrillary tangle; neuronal loss; amyloid-beta peptide; nootropic;

KW neuroprotective; antisense therapy; gene therapy; APP695-Sw-KK; mutant;

KW mutein.

XX

OS Homo sapiens.

OS Synthetic.

XX

FH Key Location/Qualifiers

FT Misc-difference 595

FT /note= "Wild type Lys substituted with Asn"

FT Misc-difference 596

FT /note= "Wild type Met substituted with Leu"

XX

PN WO200150829-A2.

XX

PD 19-JUL-2001.

XX

PF 09-MAY-2001; 2001WO-IB000799.

XX

PR 09-MAY-2001; 2001WO-IB000799.

XX

PA (BIEN/) BIENKOWSKI M J.

PA (GURN/) GURNEY M E.

PA (HEIN/) HEINRIKSON R L.

PA (PARO/) PARODI L A.

PA (YANR/) YAN R.

XX

PI Bienkowski MJ, Gurney ME, Heinrikson RL, Parodi LA, Yan R;

XX

DR WPI; 2001-483072/52.

DR N-PSDB; AAD13028.

XX

PT Novel purified polypeptide comprising fragment of mammalian aspartyl

PT protease 2, lacking Asp2 transmembrane domain and retaining beta

PT secretase activity of Asp2 useful for identifying inhibitors of Asp2

PT activity.

XX

PS Example 6; Page 147-149; 185pp; English.

XX

CC The invention relates to human aspartyl proteases (Hu-Asp), beta-amyloid

CC precursor protein (APP) isoforms and their corresponding DNA molecules.

CC Human aspartyl proteases can act as beta-secretase proteases useful for

CC treating Alzheimer's disease. APP isoforms are useful for identifying

CC modulators of amyloid-beta peptide production, for use in designing

therapeutics for the treatment and prevention of Alzheimer's disease, dementia, formation of amyloid plaques, neurofibrillary tangles, gliosis and neuronal loss. APP isoforms are also used in methods for identifying inhibitors and modulators of human Asp2 activity. The invention relates to a method for identifying agents that modulate the activity of human aspartyl protease Asp2. Amyloid-beta peptides obtained from APP are used as a means to screen in cellular assays for the inhibitors of beta- and gamma- secretase. Hu-Asp DNA fragments are useful as probes or primers in polymerase chain reactions (PCR). The probes are useful for detecting Hu-Asp nucleic acids in in vitro assays and in Northern and Southern blots. The present sequence is modified human amyloid precursor protein 695-Swedish (APP695-Sw-KK) isoform. APP695-Sw-KK isoform is obtained by addition of two Lys residues (KK motif) at the C-terminal end of APP695-Sw isoform. APP695-Sw isoform is obtained by Swedish KM-NL mutation in APP695 isoform, where Lys at position 595 is replaced with Asn, Met at position 596 is replaced with Leu. APP695-Sw-KK isoform is useful for assaying the beta-secretase activity of human aspartyl protease 2a (Hu-Asp2a) protein

XX

SQ Sequence 697 AA;

Query Match 100.0%; Score 3651; DB 4; Length 697;  
Best Local Similarity 100.0%; Pred. No. 5.1e-253;  
Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVYPQLQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPQLQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480

Qy 481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540  
 |||  
 Db 481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540

Qy 541 DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600  
 |||  
 Db 541 DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600

Qy 601 RHDSGYEVHHQKL VFFAEDVGSNKGAI IGLMVGGVVIATVIVITLVMLKKKQYTSIH HGV 660  
 |||  
 Db 601 RHDSGYEVHHQKL VFFAEDVGSNKGAI IGLMVGGVVIATVIVITLVMLKKKQYTSIH HGV 660

Qy 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697  
 |||  
 Db 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697

RESULT 5

AAE02588

ID AAE02588 standard; protein; 697 AA.

XX

AC AAE02588;

XX

DT 10-AUG-2001 (first entry)

XX

DE Human amyloid precursor protein 695-Sw-KK (APP695-Sw-KK).

XX

KW Human; alpha-secretase; amyloid precursor protein 695-Sw-KK; therapy;

KW APP695-Sw-KK; Alzheimer's disease; antialzheimer's.

XX

OS Homo sapiens.

OS Synthetic.

XX

PN WO200123533-A2.

XX

PD 05-APR-2001.

XX

PF 22-SEP-2000; 2000WO-US026080.

XX

PR 23-SEP-1999; 99US-0155493P.

PR 23-SEP-1999; 99WO-US020881.

PR 13-OCT-1999; 99US-00416901.

PR 06-DEC-1999; 99US-0169232P.

XX

PA (PHAA ) PHARMACIA & UPJOHN CO.

XX

PI Gurney M, Bienkowski MJ;

XX

DR WPI; 2001-290516/30.

DR N-PSDB; AAD06746.

XX

PT Enzymes that cleave the alpha-secretase site of the amyloid precursor protein, useful for the treatment of Alzheimer's disease.

XX

PS Example 6; Page 146-148; 189pp; English.

XX

CC The present invention relates to enzymes for cleaving the alpha-

CC secretase site of the amyloid precursor protein (APP) and methods of  
CC identifying those enzymes. The methods may be used to identify enzymes  
CC that may be used to cleave the alpha-secretase cleavage site of the APP  
CC protein. The enzymes may be used to treat or modulate the progress of  
CC Alzheimer's disease. The present sequence is human APP695-Sw-KK. This  
CC sequence contains a Sw mutation which is characterised by a KM to NL  
CC alteration at positions 595-596 and two lysine residues at the carboxyl-  
CC terminal end

XX

SQ Sequence 697 AA;

Query Match 100.0%; Score 3651; DB 4; Length 697;  
Best Local Similarity 100.0%; Pred. No. 5.1e-253;  
Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
        |||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
        |||
Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
        |||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
        |||
Db    181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDDGDEVEEEAEPEYEEATERTTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
        |||
Db    241 EADDDDEDDGDEVEEEAEPEYEEATERTTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360
        |||
Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360

Qy    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
        |||
Db    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480
        |||
Db    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480

Qy    481 EEIQDEVDELLQKEQNYSDVLANMISEPRI SYGNDALMPSLTETKTTVELLPVNGEFSL 540
        |||
Db    481 EEIQDEVDELLQKEQNYSDVLANMISEPRI SYGNDALMPSLTETKTTVELLPVNGEFSL 540

Qy    541 DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEI SEVNLD AEF 600
        |||
Db    541 DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEI SEVNLD AEF 600

Qy    601 RHDSGYEVHHQKLVFFAEDVGSNKGAI IGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660
        |||
```



Db 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHG 660

Qy 661 VEVDAAVTPEERHLSKMQONGYENPTYKFFEQMQNKK 697

Db 661 VEVDAAVTPEERHLSKMQONGYENPTYKFFEQMQNKK 697

RESULT 6

AAU06610

ID AAU06610 standard; protein; 697 AA.

XX

AC AAU06610;

XX

DT 24-OCT-2001 (first entry)

XX

DE Human Amyloid precursor protein mutant, APP695-SW-KK.

XX

KW Human; Aspartyl protease; Asp2b; beta-secretase; nootropic;

KW neuroprotective; amyloid protein precursor; APP; Alzheimer's disease;

KW amyloid-beta; Abeta; APP695-SW-KK; mutant; mutein.

XX

OS Homo sapiens.

XX

FH Key Location/Qualifiers

FT Misc-difference 595. .596

FT /note= "Wild-type Lys-Met substituted by Asn-Leu"

FT Misc-difference 696. .697

FT /note= "2 Extra Lys residues added compared to wild-type

FT APP695"

XX

PN WO200149098-A2.

XX

PD 12-JUL-2001.

XX

PF 09-MAY-2001; 2001WO-IB000798.

XX

PR 09-MAY-2001; 2001WO-IB000798.

XX

PA (BIEN/) BIENKOWSKI M J.

PA (GURN/) GURNEY M E.

PA (HEIN/) HEINRIKSON R L.

PA (PARO/) PARODI L A.

PA (YANR/) YAN R.

XX

PI Bienkowski MJ, Gurney ME, Heinrikson RL, Parodi LA, Yan R;

XX

DR WPI; 2001-502549/55.

DR N-PSDB; AAS11524.

XX

PT Novel purified polypeptide comprising fragment of mammalian aspartyl

PT protease 2, lacking Asp2 transmembrane domain and retaining beta

PT secretase activity of Asp2 useful for identifying inhibitors of Asp2

PT activity.

XX

PS Example 6; Page 147-149; 185pp; English.

XX

CC The invention relates to a purified polypeptide comprising a fragment of



Qy	361	QEKVESLEQEAAENERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAAENERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVP	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVP	480
Qy	481	EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDAIMPSTETKTTVELLPVNGEFS	540
Db	481	EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDAIMPSTETKTTVELLPVNGEFS	540
Qy	541	DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD	600
Db	541	DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD	600
Qy	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSI	660
Db	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSI	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697

RESULT 7

ABB78597

ID ABB78597 standard; protein; 697 AA.

XX

AC ABB78597;

XX

DT 16-JUL-2002 (first entry)

XX

DE Human APP695-Sw-KK protein sequence SEQ ID NO:18.

XX

KW Human; Asp-1; Asp-2; aspartyl protease; Alzheimer's disease; proteolytic;  
 KW amyloid precursor protein; APP.

XX

OS Homo sapiens.

XX

PN GB2367060-A.

XX

PD 27-MAR-2002.

XX

PF 29-OCT-2001; 2001GB-00025934.

XX

PR 23-SEP-1999; 99US-00404133.

PR 23-SEP-1999; 99US-0155493P.

PR 23-SEP-1999; 99WO-US020881.

PR 13-OCT-1999; 99US-00416901.

PR 06-DEC-1999; 99US-0169232P.

PR 22-SEP-2000; 2000GB-00023315.

XX

PA (PHAA ) PHARMACIA & UPJOHN CO.

XX

PI Bienkowski MJ, Gurney M;

XX

DR WPI; 2002-397167/43.

DR N-PSDB; ABL52464.

XX

PT Human aspartyl protease 1 substrates useful in assays to detect aspartyl  
PT protease activity, e.g. for the diagnosis of Alzheimer's disease.

XX

PS Example 6; Page 117-119; 182pp; English.

XX

CC The present invention describes a human aspartyl protease 1 (hu-Asp1)  
CC substrate (I) which comprises a peptide of no more than 50 amino acids,  
CC and which comprises the 8 amino acid sequence Gly-Leu-Ala-Leu-Ala-Leu-  
CC Glu-Pro. Also described are: (1) a method (II) for assaying hu-Asp1  
CC proteolytic activity, comprising: (a) contacting a hu-Asp1 protein with  
CC (I) under acidic conditions; and (b) determining the level of hu-Asp1  
CC proteolytic activity; (2) a purified polynucleotide (III) comprising a  
CC nucleotide sequence that hybridises under stringent conditions to the non  
CC -coding strand complementary to a defined 1804 nucleotide sequence (see  
CC ABL52456) where the nucleotide sequence encodes a polypeptide having Asp1  
CC proteolytic activity and lacks nucleotides encoding a transmembrane  
CC domain); (3) a purified polynucleotide (III') comprising a sequence that  
CC hybridises under stringent conditions to (III) (the nucleotide sequence  
CC encodes a polypeptide further lacking a pro-peptide domain corresponding  
CC to amino acids 23-62 of hu-Asp1 (see ABB78589)); (4) a vector (IV)  
CC comprising (III) or (III'); and (5) a host cell (V) transformed or  
CC transfected with (III), (III') and/or (IV). The hu-Asp1 protease  
CC substrate (I) may be used as an enzyme substrate in assays to detect  
CC aspartyl protease activity, (II) and therefore diagnose diseases  
CC associated with aberrant hu-Asp1 expression and activity such as  
CC Alzheimer's disease. Hu-Asp1 has been localised to chromosome 21, while  
CC hu-Asp2 has been localised to chromosome 11q23.3-24.1. The present  
CC sequence represents human amyloid precursor protein APP695-Sw-KK, which  
CC is given in an example from the present invention

XX

SQ Sequence 697 AA;

Query Match 100.0%; Score 3651; DB 5; Length 697;

Best Local Similarity 100.0%; Pred. No. 5.1e-253;

Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
      |||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
      |||
Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
      |||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
      |||
Db    181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
      |||
```

Db 241 EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300  
 Qy 301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360  
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||  
 Db 301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360  
 Qy 361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420  
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||  
 Db 361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420  
 Qy 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480  
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||  
 Db 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480  
 Qy 481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540  
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||  
 Db 481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540  
 Qy 541 DDLQPWHSFGADSVANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600  
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||  
 Db 541 DDLQPWHSFGADSVANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600  
 Qy 601 RHDSGYEVHHQKL VFFAEDVGSNKGAI IGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660  
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||  
 Db 601 RHDSGYEVHHQKL VFFAEDVGSNKGAI IGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660  
 Qy 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK 697  
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||  
 Db 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK 697

RESULT 8

AA88428

ID AAY88428 standard; protein; 697 AA.

XX

AC AAY88428;

XX

DT 03-AUG-2000 (first entry)

XX

DE Human APP696-KK amino acid sequence.

XX

KW Aspartyl protease; aspartase; amyloid precursor protein; APP; Asp 2;

KW Alzheimer's disease; beta secretase site; APP696-KK.

XX

OS Homo sapiens.

XX

PN WO200017369-A2.

XX

PD 30-MAR-2000.

XX

PF 23-SEP-1999; 99WO-US020881.

XX

PR 24-SEP-1998; 98US-0101594P.

XX

PA (PHAA ) PHARMACIA & UPJOHN CO.

XX

PI Gurney ME, Bienkowski MJ, Heinrikson RL, Parodi LA, Yan R;





PI Bienkowski MJ, Gurney ME, Heinrikson RL, Parodi LA, Yan R;  
 XX  
 DR WPI; 2001-502548/55.  
 DR N-PSDB; AAS11708.  
 XX  
 PT Novel purified polypeptide comprising fragment of mammalian aspartyl  
 PT protease 2, lacking Asp2 transmembrane domain and retaining beta  
 PT secretase activity of Asp2 useful for identifying inhibitors of Asp2  
 PT activity.

XX  
 PS Example 6; Page 144-146; 185pp; English.

XX  
 CC The invention relates to a novel purified polypeptide comprising a  
 CC fragment of mammalian aspartyl protease 2 (Asp2) protein which lacks the  
 CC Asp2 transmembrane domain and the Asp2 protein, and where the polypeptide  
 CC and the fragment retain the beta-secretase activity of the mammalian Asp2  
 CC protein. Also included is an isoform of amyloid protein precursor (APP)  
 CC comprising the amino acid sequence of a APP or its fragment containing an  
 CC APP cleavage site recognisable by a mammalian beta-secretase, and further  
 CC comprising two lysine residues at the carboxyl terminus of the amino acid  
 CC sequence of the mammalian APP or APP fragment. The polypeptides are used  
 CC for assaying for modulators of beta-secretase activity; identifying  
 CC agents that inhibit the APP processing activity of human Asp2 aspartyl  
 CC protease (Hu-Asp2); identifying agents that modulate the activity of Asp2  
 CC ; and for reducing cellular production of amyloid beta (Abeta) from APP.  
 CC Agents identified by the above methods are useful for treating  
 CC Alzheimer's disease; and for identifying modulators of amyloid-beta  
 CC (Abeta) peptide production, for use in designing therapeutics for the  
 CC treatment or prevention of Alzheimer's disease. Probes and primers  
 CC derived from Asp nucleic acid sequences are useful for detecting Hu-Asp  
 CC nucleic acids in in vitro assays and in Northern and Southern blots. The  
 CC present sequence represents the amino acid sequence of human amyloid  
 CC protein precursor, APP695-KK, used in the method of the invention

XX  
 SQ Sequence 697 AA;

Query Match 99.8%; Score 3643; DB 4; Length 697;  
 Best Local Similarity 99.7%; Pred. No. 1.9e-252;  
 Matches 695; Conservative 1; Mismatches 1; Indels 0; Gaps 0;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSG	TK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSG	TK	60
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG		120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG		120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR		180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR		180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE		240
Db	181	GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE		240
Qy	241	EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV		300



Db	241	 EADDDDEDDGDEVEEEAEPEYEEATERTTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Db	301	 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Db	421	 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL	540
Db	481	 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF	600
Db	541	 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMD AEF	600
Qy	601	RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV	660
Db	601	 RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK	697
Db	661	 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK	697

RESULT 10

AAE10635

ID AAE10635 standard; protein; 697 AA.

XX

AC AAE10635;

XX

DT 10-DEC-2001 (first entry)

XX

DE Human amyloid protein precursor 695-KK (APP695-KK) isoform.

XX

KW Human; aspartyl protease 1; Aspl; amyloid precursor protein; APP695-KK;

KW Alzheimer's disease; AD; dementia; neurofibrillary tangle; gliosis;

KW amyloid plaque; neuronal loss; proteolytic; nootropic; neuroprotective.

XX

OS Homo sapiens.

OS Synthetic.

XX

PN GB2357767-A.

XX

PD 04-JUL-2001.

XX

PF 22-SEP-2000; 2000GB-00023315.

XX

PR 23-SEP-1999; 99US-00404133.

PR 23-SEP-1999; 99US-0155493P.

PR 23-SEP-1999; 99WO-US020881.  
PR 13-OCT-1999; 99US-00416901.  
PR 06-DEC-1999; 99US-0169232P.

XX

PA (PHAA ) PHARMACIA & UPJOHN CO.

XX

PI Bienkowski MJ, Gurney M;

XX

DR WPI; 2001-444208/48.

DR N-PSDB; AAD17871.

XX

PT Polypeptide comprising fragments of human aspartyl protease with amyloid  
PT precursor protein processing activity and alpha-secretase activity, for  
PT identifying modulators useful in treating Alzheimer's disease.

XX

PS Example 6; Page 114-116; 187pp; English.

XX

CC The patent discloses human aspartyl protease 1 (hu-Asp1) or modified Asp1  
CC proteins which lack transmembrane domain or amino terminal domain or  
CC cytoplasmic domain and retains alpha-secretase activity and amyloid  
CC protein precursor (APP) processing activity. The proteins of the  
CC invention are useful for assaying hu-Asp1 alpha-secretase activity, which  
CC in turn is useful for identifying modulators of hu-Asp1 alpha-secretase  
CC activity, where modulators that increase hu-Asp1 alpha-secretase activity  
CC are useful for treating Alzheimer's disease (AD) which causes progressive  
CC dementia with consequent formation of amyloid plaques, neurofibrillary  
CC tangles, gliosis and neuronal loss. Hu-Asp1 protease substrate is useful  
CC for assaying hu-Asp1 proteolytic activity, by contacting hu-Asp1 protein  
CC with the substrate under acidic conditions and determining the level of  
CC hu-Asp1 proteolytic activity. The present sequence is human amyloid  
CC protein precursor 695-KK (APP695-KK) isoform which is obtained by the  
CC addition of two Lys residues (KK motif) at the C-terminus of APP695  
CC protein

XX

SQ Sequence 697 AA;

Query Match 99.8%; Score 3643; DB 4; Length 697;  
Best Local Similarity 99.7%; Pred. No. 1.9e-252;  
Matches 695; Conservative 1; Mismatches 1; Indels 0; Gaps 0;

Qy 1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGTK 60  
|  
Db 1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGTK 60  
  
Qy 61 TCIDTKEGILQYCQEVYPQLITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120  
|  
Db 61 TCIDTKEGILQYCQEVYPQLITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120  
  
Qy 121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180  
|  
Db 121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180  
  
Qy 181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240  
|  
Db 181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240  
  
Qy 241 EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

Db	241	 EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Db	301	 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA	480
Db	421	 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Db	481	 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLDAAF	600
Db	541	 DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAAF	600
Qy	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMMLKKKQYTSIHGGV	660
Db	601	 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMMLKKKQYTSIHGGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK	697
Db	661	 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK	697

RESULT 11

AAE06865

ID AAE06865 standard; protein; 697 AA.

XX

AC AAE06865;

XX

DT 23-OCT-2001 (first entry)

XX

DE Human amyloid precursor protein 695-KK (APP695-KK) isoform.

XX

KW Human; aspartyl protease; Asp; beta-amyloid precursor protein 695-KK;  
 KW beta-secretase; Alzheimer's disease; dementia; amyloid plaque; gliosis;  
 KW neurofibrillary tangle; neuronal loss; amyloid-beta peptide; nootropic;  
 KW neuroprotective; antisense therapy; gene therapy; APP695-KK; mutant;  
 KW mutein.

XX

OS Homo sapiens.

XX

PN WO200150829-A2.

XX

PD 19-JUL-2001.

XX

PF 09-MAY-2001; 2001WO-IB000799.

XX

PR 09-MAY-2001; 2001WO-IB000799.

XX  
PA (BIEN/) BIENKOWSKI M J.  
PA (GURN/) GURNEY M E.  
PA (HEIN/) HEINRIKSON R L.  
PA (PARO/) PARODI L A.  
PA (YANR/) YAN R.  
XX  
PI Bienkowski MJ, Gurney ME, Heinrikson RL, Parodi LA, Yan R;  
XX  
DR WPI; 2001-483072/52.  
DR N-PSDB; AAD13027.  
XX  
PT Novel purified polypeptide comprising fragment of mammalian aspartyl  
PT protease 2, lacking Asp2 transmembrane domain and retaining beta  
PT secretase activity of Asp2 useful for identifying inhibitors of Asp2  
PT activity.  
XX  
PS Example 6; Page 144-146; 185pp; English.  
XX  
CC The invention relates to human aspartyl proteases (Hu-Asp), beta-amyloid  
CC precursor protein (APP) isoforms and their corresponding DNA molecules.  
CC Human aspartyl proteases can act as beta-secretase proteases useful for  
CC treating Alzheimer's disease. APP isoforms are useful for identifying  
CC modulators of amyloid-beta peptide production, for use in designing  
CC therapeutics for the treatment and prevention of Alzheimer's disease,  
CC dementia, formation of amyloid plaques, neurofibrillary tangles, gliosis  
CC and neuronal loss. APP isoforms are also used in methods for identifying  
CC inhibitors and modulators of human Asp2 activity. The invention relates  
CC to a method for identifying agents that modulate the activity of human  
CC aspartyl protease Asp2. Amyloid-beta peptides obtained from APP are used  
CC as a means to screen in cellular assays for the inhibitors of beta- and  
CC gamma- secretase. Hu-Asp DNA fragments are useful as probes or primers in  
CC polymerase chain reactions (PCR). The probes are useful for detecting Hu-  
CC Asp nucleic acids in in vitro assays and in Northern and Southern blots.  
CC The present sequence is modified human amyloid precursor protein 695-KK  
CC (APP695-KK) isoform. APP695-KK isoform is obtained by addition of two Lys  
CC residues (KK motif) at the C-terminal end of APP695 isoform  
XX  
SQ Sequence 697 AA;

Query Match 99.8%; Score 3643; DB 4; Length 697;  
Best Local Similarity 99.7%; Pred. No. 1.9e-252;  
Matches 695; Conservative 1; Mismatches 1; Indels 0; Gaps 0;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSG	TK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSG	TK	60
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVI	PYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVI	PYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDK	FR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDK	FR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEE		240

Db	181		240
Qy	241	EADDDDEDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241		300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Db	301		360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361		420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA	480
Db	421		480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Db	481		540
Qy	541	DDLQPWHSFGADSVANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVNLDADF	600
Db	541		600
Qy	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMMLKKKQYTSIHGGV	660
Db	601		660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697
Db	661		697

RESULT 12

AAE02587

ID AAE02587 standard; protein; 697 AA.

XX

AC AAE02587;

XX

DT 10-AUG-2001 (first entry)

XX

DE Human amyloid precursor protein 695-KK (APP695-KK).

XX

KW Human; alpha-secretase; amyloid precursor protein 695-KK; APP695-KK;  
therapy; Alzheimer's disease; antialzheimer's.

XX

OS Homo sapiens.

OS Synthetic.

XX

PN WO200123533-A2.

XX

PD 05-APR-2001.

XX

PF 22-SEP-2000; 2000WO-US026080.



```

Db      361  |||||
Qy      421  KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480
Db      421  |||||
Qy      481  EEIQDEVDELLQKEQNYSDVLANMISEPRI SYGNDALMPSLTETKTTVELLPVNGEFSL 540
Db      481  |||||
Qy      541  DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600
Db      541  |||||
Qy      601  RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660
Db      601  |||||
Qy      661  VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK 697
Db      661  |||||

```

RESULT 13

AAU06609

ID AAU06609 standard; protein; 697 AA.

XX

AC AAU06609;

XX

DT 24-OCT-2001 (first entry)

XX

DE Human Amyloid precursor protein mutant, APP695-KK.

XX

KW Human; Aspartyl protease; Asp2b; beta-secretase; nootropic;

KW neuroprotective; amyloid protein precursor; APP; Alzheimer's disease;

KW amyloid-beta; Abeta; APP695-KK; mutant; mutein.

XX

OS Homo sapiens.

XX

FH Key Location/Qualifiers

FT Misc-difference 696. .697

FT /note= "2 Extra Lys residues added compared to wild-type  
APP695"

XX

PN WO200149098-A2.

XX

PD 12-JUL-2001.

XX

PF 09-MAY-2001; 2001WO-IB000798.

XX

PR 09-MAY-2001; 2001WO-IB000798.

XX

PA (BIEN/) BIENKOWSKI M J.

PA (GURN/) GURNEY M E.

PA (HEIN/) HEINRIKSON R L.

PA (PARO/) PARODI L A.

XX

XX

DR

XX

XX

XX

XX

Best Local Similarity 99.7%; Pred. No. 1.9e-252;

Db

Db



Db	121	 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	 GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	 EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Db	301	 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Db	421	 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Db	481	 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNDAEF	600
Db	541	 DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Qy	601	RHDSGYEVHHQKLVFVFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV	660
Db	601	 RHDSGYEVHHQKLVFVFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697
Db	661	 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697

RESULT 14

ABB78596

ID ABB78596 standard; protein; 697 AA.

XX

AC ABB78596;

XX

DT 16-JUL-2002 (first entry)

XX

DE Human APP695-KK protein sequence SEQ ID NO:16.

XX

KW Human; Asp-1; Asp-2; aspartyl protease; Alzheimer's disease; proteolytic;  
KW amyloid precursor protein; APP.

XX

OS Homo sapiens.

XX

PN GB2367060-A.

XX

PD 27-MAR-2002.

XX

PF 29-OCT-2001; 2001GB-00025934.

XX

PR 23-SEP-1999; 99US-00404133.

PR 23-SEP-1999; 99US-0155493P.

PR 23-SEP-1999; 99WO-US020881.

PR 13-OCT-1999; 99US-00416901.

PR 06-DEC-1999; 99US-0169232P.

PR 22-SEP-2000; 2000GB-00023315.

XX

PA (PHAA ) PHARMACIA & UPJOHN CO.

XX

PI Bienkowski MJ, Gurney M;

XX

DR WPI; 2002-397167/43.

DR N-PSDB; ABL52463.

XX

PT Human aspartyl protease 1 substrates useful in assays to detect aspartyl  
PT protease activity, e.g. for the diagnosis of Alzheimer's disease.

XX

PS Example 6; Page 114-116; 182pp; English.

XX

CC The present invention describes a human aspartyl protease 1 (hu-Asp1)  
CC substrate (I) which comprises a peptide of no more than 50 amino acids,  
CC and which comprises the 8 amino acid sequence Gly-Leu-Ala-Leu-Ala-Leu-  
CC Glu-Pro. Also described are: (1) a method (II) for assaying hu-Asp1  
CC proteolytic activity, comprising: (a) contacting a hu-Asp1 protein with  
CC (I) under acidic conditions; and (b) determining the level of hu-Asp1  
CC proteolytic activity; (2) a purified polynucleotide (III) comprising a  
CC nucleotide sequence that hybridises under stringent conditions to the non  
CC -coding strand complementary to a defined 1804 nucleotide sequence (see  
CC ABL52456) where the nucleotide sequence encodes a polypeptide having Asp1  
CC proteolytic activity and lacks nucleotides encoding a transmembrane  
CC domain); (3) a purified polynucleotide (III') comprising a sequence that  
CC hybridises under stringent conditions to (III) (the nucleotide sequence  
CC encodes a polypeptide further lacking a pro-peptide domain corresponding  
CC to amino acids 23-62 of hu-Asp1 (see ABB78589)); (4) a vector (IV)  
CC comprising (III) or (III'); and (5) a host cell (V) transformed or  
CC transfected with (III), (III') and/or (IV). The hu-Asp1 protease  
CC substrate (I) may be used as an enzyme substrate in assays to detect  
CC aspartyl protease activity, (II) and therefore diagnose diseases  
CC associated with aberrant hu-Asp1 expression and activity such as  
CC Alzheimer's disease. Hu-Asp1 has been localised to chromosome 21, while  
CC hu-Asp2 has been localised to chromosome 11q23.3-24.1. The present  
CC sequence represents human amyloid precursor protein APP695-KK, which is  
CC given in an example from the present invention

XX

SQ Sequence 697 AA;

Query Match 99.8%; Score 3643; DB 5; Length 697;

Best Local Similarity 99.7%; Pred. No. 1.9e-252;

Matches 695; Conservative 1; Mismatches 1; Indels 0; Gaps 0;

Qy 1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

|||||

Db 1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDDGDEVEEEAEEPYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDDGDEVEEEAEEPYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF	600
Db	541	DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMD AEF	600
Qy	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIH HGV	660
Db	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIH HGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697

RESULT 15

AA Y88435

ID AAY88435 standard; protein; 695 AA.

XX

AC AAY88435;

XX

DT 03-AUG-2000 (first entry)

XX

DE Human APP695-sw variant amino acid sequence.

XX

KW Aspartyl protease; aspartase; amyloid precursor protein; APP; Asp 2;

KW Alzheimer's disease; beta secretase site.  
XX  
OS Homo sapiens.  
XX  
PN WO200017369-A2.  
XX  
PD 30-MAR-2000.  
XX  
PF 23-SEP-1999; 99WO-US020881.  
XX  
PR 24-SEP-1998; 98US-0101594P.  
XX  
PA (PHAA ) PHARMACIA & UPJOHN CO.  
XX  
PI Gurney ME, Bienkowski MJ, Heinrikson RL, Parodi LA, Yan R;  
XX  
DR WPI; 2000-303209/26.  
DR N-PSDB; AAA15672.  
XX  
PT New enzyme designated human aspartase useful in research into Alzheimer's  
PT Disease is capable of cleaving amyloid protein precursor at the beta  
PT secretase site to produce amyloid beta peptide.  
XX  
PS Example 6; Page 125-129; 183pp; English.  
XX  
CC This sequence represents a human amyloid precursor protein 695 (APP695)  
CC variant amino acid sequence. The sequence is used in an example of the  
CC invention, showing that modification of APP can increase beta amyloid  
CC peptide processing. The invention relates to a protease (e.g. Asp2)  
CC capable of cleaving the beta secretase site of amyloid precursor protein  
CC (APP). The protease contains a sequence encoding the amino acid sequence  
CC DTG and a sequence encoding DSG or DTG separated by 100-300 amino acids.  
CC When mutated the APP gene causes an autosomal dominant form of  
CC Alzheimer's disease. APP localises to the cell surface membrane and have  
CC a single C-terminal transmembrane domain. Proteolytic processing of APP  
CC produces the amyloid beta protein, which is possibly very important in  
CC Alzheimer's disease. The invention includes a nucleotide sequence  
CC encoding the protease, a vector containing the nucleotide sequence, and a  
CC cell line comprising the vector. Methods for screening for inhibitors of  
CC beta secretase activity are also given in the invention. The human  
CC aspartase protein and nucleotide sequences and the methods for  
CC identifying inhibitors of the protease, are useful in the treatment of  
CC and research in to Alzheimer's disease  
XX  
SQ Sequence 695 AA;

Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDDEDGDEVEEEAEEPYEEATERTTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDDEDGDEVEEEAEEPYEEATERTTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLDADF	600
Db	541	DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLDADF	600
Qy	601	RHDSGYEVHHQKLFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV	660
Db	601	RHDSGYEVHHQKLFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN	695
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN	695

Search completed: July 26, 2004, 12:44:00  
 Job time : 51.3333 secs

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OM protein - protein search, using sw model

Run on: July 26, 2004, 12:41:23 ; Search time 15 Seconds  
(without alignments)  
2398.887 Million cell updates/sec

Title: US-09-806-194A-18  
Perfect score: 3651  
Sequence: 1 MLPGLALLLLAAWTARALEV.....QQNGYENPTYKFFEQMKNKK 697

Scoring table: BLOSUM62  
Gapop 10.0 , Gapext 0.5

Searched: 389414 seqs, 51625971 residues

Total number of hits satisfying chosen parameters: 389414

Minimum DB seq length: 0  
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%  
Maximum Match 100%  
Listing first 45 summaries

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3: /cgn2\_6/ptodata/2/iaa/6A\_COMB.pep:\*  
4: /cgn2\_6/ptodata/2/iaa/6B\_COMB.pep:\*  
5: /cgn2\_6/ptodata/2/iaa/PCTUS\_COMB.pep:\*  
6: /cgn2\_6/ptodata/2/iaa/backfiles1.pep:\*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	%		DB	ID	Description
		Query Match	Length			
1	3651	100.0	697	4	US-09-548-372D-18	Sequence 18, Appl
2	3651	100.0	697	4	US-09-548-367D-18	Sequence 18, Appl
3	3651	100.0	697	4	US-09-551-853D-18	Sequence 18, Appl
4	3643	99.8	697	4	US-09-548-372D-16	Sequence 16, Appl
5	3643	99.8	697	4	US-09-548-367D-16	Sequence 16, Appl
6	3643	99.8	697	4	US-09-551-853D-16	Sequence 16, Appl
7	3641	99.7	695	4	US-09-548-372D-12	Sequence 12, Appl
8	3641	99.7	695	4	US-09-548-367D-12	Sequence 12, Appl
9	3641	99.7	695	4	US-09-551-853D-12	Sequence 12, Appl
10	3638	99.6	697	4	US-09-548-372D-20	Sequence 20, Appl
11	3638	99.6	697	4	US-09-548-367D-20	Sequence 20, Appl

12	3638	99.6	697	4	US-09-551-853D-20	Sequence 20, Appl
13	3633	99.5	695	1	US-08-123-702-2	Sequence 2, Appli
14	3633	99.5	695	2	US-08-104-165-1	Sequence 1, Appli
15	3633	99.5	695	3	US-08-464-250-1	Sequence 1, Appli
16	3633	99.5	695	4	US-08-464-250-1	Sequence 1, Appli
17	3633	99.5	695	4	US-09-458-481B-7	Sequence 7, Appli
18	3633	99.5	695	4	US-09-458-481B-8	Sequence 8, Appli
19	3633	99.5	695	4	US-09-548-372D-10	Sequence 10, Appl
20	3633	99.5	695	4	US-09-548-367D-10	Sequence 10, Appl
21	3633	99.5	695	4	US-09-551-853D-10	Sequence 10, Appl
22	3633	99.5	695	4	US-09-415-099-6	Sequence 6, Appli
23	3633	99.5	695	6	5218100-2	Patent No. 5218100
24	3628	99.4	695	4	US-09-548-372D-14	Sequence 14, Appl
25	3628	99.4	695	4	US-09-548-367D-14	Sequence 14, Appl
26	3628	99.4	695	4	US-09-551-853D-14	Sequence 14, Appl
27	3627	99.3	694	1	US-08-339-152A-18	Sequence 18, Appl
28	3627	99.3	694	2	US-08-007-999B-5	Sequence 5, Appli
29	3627	99.3	694	2	US-08-689-276A-5	Sequence 5, Appli
30	3621	99.2	695	1	US-08-371-930-27	Sequence 27, Appl
31	3621	99.2	695	5	PCT-US94-01712-27	Sequence 27, Appl
32	3609	98.8	695	1	US-08-339-152A-30	Sequence 30, Appl
33	3604	98.7	753	4	US-09-548-372D-61	Sequence 61, Appl
34	3604	98.7	753	4	US-09-548-367D-61	Sequence 61, Appl
35	3604	98.7	753	4	US-09-551-853D-61	Sequence 61, Appl
36	3594	98.4	751	1	US-08-123-702-4	Sequence 4, Appli
37	3594	98.4	751	2	US-08-104-165-2	Sequence 2, Appli
38	3594	98.4	751	2	US-08-422-333-2	Sequence 2, Appli
39	3594	98.4	751	2	US-08-422-333-21	Sequence 21, Appl
40	3594	98.4	751	3	US-08-464-250-2	Sequence 2, Appli
41	3594	98.4	751	4	US-08-464-250-2	Sequence 2, Appli
42	3594	98.4	751	4	US-08-832-867-5	Sequence 5, Appli
43	3594	98.4	751	4	US-09-548-372D-57	Sequence 57, Appl
44	3594	98.4	751	4	US-09-548-367D-57	Sequence 57, Appl
45	3594	98.4	751	4	US-09-551-853D-57	Sequence 57, Appl

#### ALIGNMENTS

```

RESULT 1
US-09-548-372D-18
; Sequence 18, Application US/09548372D
; Patent No. 6420534
; GENERAL INFORMATION:
; APPLICANT: GURNEY ET AL.
; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR
AND USES
; TITLE OF INVENTION: THEREOF
; FILE REFERENCE: 29915/6280I
; CURRENT APPLICATION NUMBER: US/09/548,372D
; CURRENT FILING DATE: 2000-04-12
; PRIOR APPLICATION NUMBER: US 60/155,493
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: US 09/404,133
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23

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; PRIOR APPLICATION NUMBER: US 60/101,594  
; PRIOR FILING DATE: 1998-09-24  
; NUMBER OF SEQ ID NOS: 73  
; SOFTWARE: PatentIn version 3.1  
; SEQ ID NO 18  
; LENGTH: 697  
; TYPE: PRT  
; ORGANISM: Homo sapiens  
US-09-548-372D-18

Query Match 100.0%; Score 3651; DB 4; Length 697;  
Best Local Similarity 100.0%; Pred. No. 4.6e-268;  
Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG	120
Db	61	TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE	240
Qy	241	EADDDDEDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF	600
Db	541	DDLQPWHSFGADSVANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF	600
Qy	601	RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV	660
Db	601	RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV	660



Qy           661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697  
             | | | | | | | | | | | | | | | | | | | | | |  
Db           661 VEVDAAVTPEERHLSKMOONGYENPTYKFFEOMONKK 697

Qy 301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360  
 |||  
 Db 301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360

Qy 361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420  
 |||  
 Db 361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480  
 |||  
 Db 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480

Qy 481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540  
 |||  
 Db 481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540

Qy 541 DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLDADF 600  
 |||  
 Db 541 DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLDADF 600

Qy 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV 660  
 |||  
 Db 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV 660

Qy 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK 697  
 |||  
 Db 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK 697

# RESULT 3

US-09-551-853D-18

; Sequence 18, Application US/09551853D

; Patent No. 6500667

; GENERAL INFORMATION:

; APPLICANT: GURNEY ET AL.

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR AND USES

; TITLE OF INVENTION: THEREOF

; FILE REFERENCE: 29915/6280L

; CURRENT APPLICATION NUMBER: US/09/551,853D

; CURRENT FILING DATE: 2000-04-18

; PRIOR APPLICATION NUMBER: US 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 73

; SOFTWARE: PatentIn version 3.1

; SEQ ID NO 18

; LENGTH: 697

; TYPE: PRT

; ORGANISM: Homo sapiens

US-09-551-853D-18

Query Match 100.0%; Score 3651; DB 4; Length 697;  
Best Local Similarity 100.0%; Pred. No. 4.6e-268;  
Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEEEE	240
Qy	241	EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTSVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTSVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVNDAEF	600
Db	541	DDLQPWHSFGADSVANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVNDAEF	600
Qy	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLMLKKKQYTSIHGCV	660
Db	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLMLKKKQYTSIHGCV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697

RESULT 4  
US-09-548-372D-16  
; Sequence 16, Application US/09548372D

```

; Patent No. 6420534
; GENERAL INFORMATION:
; APPLICANT: GURNEY ET AL.
; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR
AND USES
; TITLE OF INVENTION: THEREOF
; FILE REFERENCE: 29915/6280I
; CURRENT APPLICATION NUMBER: US/09/548,372D
; CURRENT FILING DATE: 2000-04-12
; PRIOR APPLICATION NUMBER: US 60/155,493
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: US 09/404,133
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: US 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 73
; SOFTWARE: PatentIn version 3.1
; SEQ ID NO 16
; LENGTH: 697
; TYPE: PRT
; ORGANISM: Homo sapiens
US-09-548-372D-16

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Query Match          99.8%; Score 3643; DB 4; Length 697;
Best Local Similarity 99.7%; Pred. No. 1.9e-267;
Matches 695; Conservative 1; Mismatches 1; Indels 0; Gaps 0;

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Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
        |||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
        |||
Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
        |||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDDSVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
        |||
Db    181 GVEFVCCPLAEESDNVDSADAEEDDSVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
        |||
Db    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360
        |||
Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360

Qy    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
        |||
Db    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

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Qy 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480  
 |||  
 Db 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480

Qy 481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL 540  
 |||  
 Db 481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL 540

Qy 541 DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600  
 ||| :|||  
 Db 541 DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEISEVKMD AEF 600

Qy 601 RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660  
 |||  
 Db 601 RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660

Qy 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK 697  
 |||  
 Db 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK 697

RESULT 5

US-09-548-367D-16

; Sequence 16, Application US/09548367D

; Patent No. 6440698

; GENERAL INFORMATION:

; APPLICANT: GURNEY ET AL.

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR AND USES

; TITLE OF INVENTION: THEREOF

; FILE REFERENCE: 29915/6280H

; CURRENT APPLICATION NUMBER: US/09/548,367D

; CURRENT FILING DATE: 2000-04-12

; PRIOR APPLICATION NUMBER: US 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 73

; SOFTWARE: PatentIn version 3.1

; SEQ ID NO 16

; LENGTH: 697

; TYPE: PRT

; ORGANISM: Homo sapiens

US-09-548-367D-16

Query Match 99.8%; Score 3643; DB 4; Length 697;

Best Local Similarity 99.7%; Pred. No. 1.9e-267;

Matches 695; Conservative 1; Mismatches 1; Indels 0; Gaps 0;

Qy 1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60  
 |||

Db 1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVI	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVI	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDGDEVEEEAEEPYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDGDEVEEEAEEPYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF	600
		:	
Db	541	DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMD AEF	600
Qy	601	RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV	660
Db	601	RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK	697
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK	697

RESULT 6

US-09-551-853D-16

; Sequence 16, Application US/09551853D

; Patent No. 6500667

; GENERAL INFORMATION:

; APPLICANT: GURNEY ET AL.

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR AND USES

; TITLE OF INVENTION: THEREOF

; FILE REFERENCE: 29915/6280L

; CURRENT APPLICATION NUMBER: US/09/551,853D

; CURRENT FILING DATE: 2000-04-18

; PRIOR APPLICATION NUMBER: US 60/155,493  
 ; PRIOR FILING DATE: 1999-09-23  
 ; PRIOR APPLICATION NUMBER: US 09/404,133  
 ; PRIOR FILING DATE: 1999-09-23  
 ; PRIOR APPLICATION NUMBER: PCT/US99/20881  
 ; PRIOR FILING DATE: 1999-09-23  
 ; PRIOR APPLICATION NUMBER: US 60/101,594  
 ; PRIOR FILING DATE: 1998-09-24  
 ; NUMBER OF SEQ ID NOS: 73  
 ; SOFTWARE: PatentIn version 3.1  
 ; SEQ ID NO 16  
 ; LENGTH: 697  
 ; TYPE: PRT  
 ; ORGANISM: Homo sapiens  
 US-09-551-853D-16

Query Match 99.8%; Score 3643; DB 4; Length 697;  
 Best Local Similarity 99.7%; Pred. No. 1.9e-267;  
 Matches 695; Conservative 1; Mismatches 1; Indels 0; Gaps 0;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE	240
Qy	241	EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTSVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTSVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVPAANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF	600

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Db      541 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600
Qy      601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660
Db      601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660
Qy      661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697
Db      661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697

```

RESULT 7

US-09-548-372D-12

; Sequence 12, Application US/09548372D

; Patent No. 6420534

; GENERAL INFORMATION:

; APPLICANT: GURNEY ET AL.

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR AND USES

; TITLE OF INVENTION: THEREOF

; FILE REFERENCE: 29915/6280I

; CURRENT APPLICATION NUMBER: US/09/548,372D

; CURRENT FILING DATE: 2000-04-12

; PRIOR APPLICATION NUMBER: US 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 73

; SOFTWARE: PatentIn version 3.1

; SEQ ID NO 12

; LENGTH: 695

; TYPE: PRT

; ORGANISM: Homo sapiens

US-09-548-372D-12

Query Match 99.7%; Score 3641; DB 4; Length 695;

Best Local Similarity 100.0%; Pred. No. 2.6e-267;

Matches 695; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGTK 60
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGTK 60
Qy      61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
Db      61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
Qy      121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
Db      121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
Qy      181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE 240

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Db	181		240
Qy	241	EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTSVEEVVRVPTTAASTPDAV	300
Db	241		300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Db	301		360
Qy	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361		420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Db	421		480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Db	481		540
Qy	541	DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF	600
Db	541		600
Qy	601	RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIH HGV	660
Db	601		660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QN	695
Db	661		695

RESULT 8

US-09-548-367D-12

; Sequence 12, Application US/09548367D

; Patent No. 6440698

; GENERAL INFORMATION:

; APPLICANT: GURNEY ET AL.

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR AND USES

; TITLE OF INVENTION: THEREOF

; FILE REFERENCE: 29915/6280H

; CURRENT APPLICATION NUMBER: US/09/548,367D

; CURRENT FILING DATE: 2000-04-12

; PRIOR APPLICATION NUMBER: US 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 73

; SOFTWARE: PatentIn version 3.1  
; SEQ ID NO 12  
; LENGTH: 695  
; TYPE: PRT  
; ORGANISM: Homo sapiens  
US-09-548-367D-12

Query Match 99.7%; Score 3641; DB 4; Length 695;  
Best Local Similarity 100.0%; Pred. No. 2.6e-267;  
Matches 695; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
        |||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG 120
        |||
Db     61 TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
        |||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
        |||
Db    181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
        |||
Db    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360
        |||
Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360

Qy    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
        |||
Db    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480
        |||
Db    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480

Qy    481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL 540
        |||
Db    481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL 540

Qy    541 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600
        |||
Db    541 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600

Qy    601 RHDSGYEVHHQKL VFFAEDVGSNKGAI IGLMVGGVVIATVIVITL VMLKKKQYTSIHHGV 660
        |||
Db    601 RHDSGYEVHHQKL VFFAEDVGSNKGAI IGLMVGGVVIATVIVITL VMLKKKQYTSIHHGV 660

Qy    661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QN 695
        |||
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Db 301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360

Qy 361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420  
 |||

Db 361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480  
 |||

Db 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480

Qy 481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540  
 |||

Db 481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540

Qy 541 DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600  
 |||

Db 541 DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600

Qy 601 RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV 660  
 |||

Db 601 RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV 660

Qy 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695  
 |||

Db 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695

RESULT 10

US-09-548-372D-20

; Sequence 20, Application US/09548372D

; Patent No. 6420534

; GENERAL INFORMATION:

; APPLICANT: GURNEY ET AL.

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR AND USES

; TITLE OF INVENTION: THEREOF

; FILE REFERENCE: 29915/6280I

; CURRENT APPLICATION NUMBER: US/09/548,372D

; CURRENT FILING DATE: 2000-04-12

; PRIOR APPLICATION NUMBER: US 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 73

; SOFTWARE: PatentIn version 3.1

; SEQ ID NO 20

; LENGTH: 697

; TYPE: PRT

; ORGANISM: Homo sapiens

US-09-548-372D-20

Query Match 99.6%; Score 3638; DB 4; Length 697;  
 Best Local Similarity 99.6%; Pred. No. 4.4e-267;

Matches 694; Conservative 1; Mismatches 2; Indels 0; Gaps 0;

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Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
      |||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
      |||
Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
      |||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEEEE 240
      |||
Db    181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEEEE 240

Qy    241 EADDDDEDDGDEVEEEAEPEYEEATERTTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
      |||
Db    241 EADDDDEDDGDEVEEEAEPEYEEATERTTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAERQAKNLPKADKKAVIQHF 360
      |||
Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAERQAKNLPKADKKAVIQHF 360

Qy    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
      |||
Db    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480
      |||
Db    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480

Qy    481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540
      |||
Db    481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540

Qy    541 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600
      |||
Db    541 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMD AEF 600

Qy    601 RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITL VMLKKKQYTSIHHGV 660
      |||
Db    601 RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIFITL VMLKKKQYTSIHHGV 660

Qy    661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK 697
      |||
Db    661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK 697

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RESULT 11

US-09-548-367D-20

; Sequence 20, Application US/09548367D

; Patent No. 6440698

; GENERAL INFORMATION:

; APPLICANT: GURNEY ET AL.

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; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR
AND USES
; TITLE OF INVENTION: THEREOF
; FILE REFERENCE: 29915/6280H
; CURRENT APPLICATION NUMBER: US/09/548,367D
; CURRENT FILING DATE: 2000-04-12
; PRIOR APPLICATION NUMBER: US 60/155,493
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: US 09/404,133
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: US 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 73
; SOFTWARE: PatentIn version 3.1
; SEQ ID NO 20
; LENGTH: 697
; TYPE: PRT
; ORGANISM: Homo sapiens
US-09-548-367D-20

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Query Match          99.6%; Score 3638; DB 4; Length 697;
Best Local Similarity 99.6%; Pred. No. 4.4e-267;
Matches 694; Conservative 1; Mismatches 2; Indels 0; Gaps 0;

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Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDDEDGDEVEEEAAEPYEEATERTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV 300
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    241 EADDDDEDDEDGDEVEEEAAEPYEEATERTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360

Qy    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480

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Qy      481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTLTETKTTVELLPVNGEFSL 540
        |||
Db      481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTLTETKTTVELLPVNGEFSL 540

Qy      541 DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600
        |||
Db      541 DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEISEVKMD AEF 600

Qy      601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660
        |||
Db      601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHHGV 660

Qy      661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK 697
        |||
Db      661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK 697

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# RESULT 12

US-09-551-853D-20

; Sequence 20, Application US/09551853D

; Patent No. 6500667

; GENERAL INFORMATION:

; APPLICANT: GURNEY ET AL.

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR AND USES

; TITLE OF INVENTION: THEREOF

; FILE REFERENCE: 29915/6280L

; CURRENT APPLICATION NUMBER: US/09/551,853D

; CURRENT FILING DATE: 2000-04-18

; PRIOR APPLICATION NUMBER: US 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 73

; SOFTWARE: PatentIn version 3.1

; SEQ ID NO 20

; LENGTH: 697

; TYPE: PRT

; ORGANISM: Homo sapiens

US-09-551-853D-20

Query Match 99.6%; Score 3638; DB 4; Length 697;

Best Local Similarity 99.6%; Pred. No. 4.4e-267;

Matches 694; Conservative 1; Mismatches 2; Indels 0; Gaps 0;

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Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGR LNMHMNVQNGKWDSDPSG TK 60
        |||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGR LNMHMNVQNGKWDSDPSG TK 60

Qy      61 TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
        |||
Db      61 TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

```

Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMP SLTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMP SLTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF	600
		:	
Db	541	DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMD AEF	600
Qy	601	RHD SGYEVHHQKL VFFAEDVGSNKGAI IGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV	660
Db	601	RHD SGYEVHHQKL VFFAEDVGSNKGAI IGLMVGGVVIATVIFITLVMLKKKQYTSIHHGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK	697
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK	697

RESULT 13

US-08-123-702-2

; Sequence 2, Application US/08123702

; Patent No. 5604131

; GENERAL INFORMATION:

; APPLICANT: Wadsworth, Samuel

; APPLICANT: Snyder, Benjamin

; APPLICANT: Reddy, Vermuri, B.

; APPLICANT: Wei, Chamer

; TITLE OF INVENTION: A cDNA Genomic Hybrid Sequence Encoding APP770

; Patent No. 5604131

; TITLE OF INVENTION: Containing a Genomic DNA Insert of the KI and OX-2 Regions

; NUMBER OF SEQUENCES: 45

; CORRESPONDENCE ADDRESS:





Db 301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360

Qy 361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420  
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Db 361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA 480  
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Db 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA 480

Qy 481 EEIQDEVDELLQKEQNYSDVLANMISEPRI SYGNDALMPSLTETKTTVELLPVNGEFSL 540  
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Db 481 EEIQDEVDELLQKEQNYSDVLANMISEPRI SYGNDALMPSLTETKTTVELLPVNGEFSL 540

Qy 541 DDLQPPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600  
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Db 541 DDLQPPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMD AEF 600

Qy 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660  
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Db 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660

Qy 661 VEVDAAVTPEERHLSKMQONGYENPTYKFFEQMQN 695  
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Db 661 VEVDAAVTPEERHLSKMQONGYENPTYKFFEQMQN 695

RESULT 14

US-08-104-165-1

; Sequence 1, Application US/08104165

; Patent No. 5877015

; GENERAL INFORMATION:

; APPLICANT: HARDY, John Anthony

; APPLICANT: GOATE, Alison Mary

; APPLICANT: MULLAN, Michael John

; APPLICANT: CHARTIER-HARLIN, Marie-Christine

; APPLICANT: OWEN, Michael John

; TITLE OF INVENTION: Test and Model for Alzheimer's Disease

; NUMBER OF SEQUENCES: 44

; CORRESPONDENCE ADDRESS:

; ADDRESSEE: Townsend and Townsend Khourie and Crew

; STREET: 379 Lytton Avenue

; CITY: Palo Alto

; STATE: California

; COUNTRY: US

; ZIP: 94301

; COMPUTER READABLE FORM:

; MEDIUM TYPE: Floppy Disk

; COMPUTER: IBM PC compatible

; OPERATING SYSTEM: PC-DOS/MS-DOS

; CURRENT APPLICATION DATA:

; APPLICATION NUMBER: US/08/104,165

; FILING DATE: 21-JAN-1992

; CLASSIFICATION: 435

; PRIOR APPLICATION DATA:

; APPLICATION NUMBER: 9101307.8

; FILING DATE: 21-JAN-1991

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; APPLICATION NUMBER: 9118445.7
; FILING DATE: 28-AUG-1991
; ATTORNEY/AGENT INFORMATION:
; NAME: Liebeschuetz, Joe
; REGISTRATION NUMBER: 37,505
; REFERENCE/DOCKET NUMBER: 16163-000100
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: (415) 326-2400
; TELEFAX: (415) 326-2422
; INFORMATION FOR SEQ ID NO: 1:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 695 amino acids
; TYPE: amino acid
; STRANDEDNESS: single
; TOPOLOGY: linear
; MOLECULE TYPE: protein
US-08-104-165-1

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Query Match          99.5%; Score 3633; DB 2; Length 695;
Best Local Similarity 99.7%; Pred. No. 1.1e-266;
Matches 693; Conservative 1; Mismatches 1; Indels 0; Gaps 0;

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Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
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Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
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Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
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Db    181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
        |||
Db    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360
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Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360

Qy    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
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Db    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

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        |||
Db    481 EEIQDEVDELLOKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540

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Qy 541 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600  
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Qy 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVM LKKKQYTSIH HGV 660  
 ||| :|||  
 Db 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVM LKKKQYTSIH HGV 660

Qy 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFE QMQN 695  
 ||| :|||  
 Db 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFE QMQN 695

RESULT 15

US-08-464-250-1

; Sequence 1, Application US/08464250

; Patent No. 6107542

; GENERAL INFORMATION:

; APPLICANT: HARDY, John Anthony

; APPLICANT: GOATE, Alison Mary

; APPLICANT: MULLAN, Michael John

; APPLICANT: CHARTIER-HARLIN, Marie-Christine

; APPLICANT: OWEN, Michael John

; TITLE OF INVENTION: Test and Model for Alzheimer's Disease

; NUMBER OF SEQUENCES: 44

; CORRESPONDENCE ADDRESS:

; ADDRESSEE: Townsend and Townsend Khourie and Crew

; STREET: 379 Lytton Avenue

; CITY: Palo Alto

; STATE: California

; COUNTRY: US

; ZIP: 94301

; COMPUTER READABLE FORM:

; MEDIUM TYPE: Floppy Disk

; COMPUTER: IBM PC compatible

; OPERATING SYSTEM: PC-DOS/MS-DOS

; CURRENT APPLICATION DATA:

; APPLICATION NUMBER: US/08/464,250

; FILING DATE: 05-JUN-1995

; CLASSIFICATION: 435

; PRIOR APPLICATION DATA:

; APPLICATION NUMBER: 08/104,165

; FILING DATE: 21-JAN-1992

; APPLICATION NUMBER: 9101307.8

; FILING DATE: 21-JAN-1991

; APPLICATION NUMBER: 9118445.7

; FILING DATE: 28-AUG-1991

; ATTORNEY/AGENT INFORMATION:

; NAME: Liebeschuetz, Joe

; REGISTRATION NUMBER: 37,505

; REFERENCE/DOCKET NUMBER: 16163-000100

; TELECOMMUNICATION INFORMATION:

; TELEPHONE: (415) 326-2400

; TELEFAX: (415) 326-2422

; INFORMATION FOR SEQ ID NO: 1:

; SEQUENCE CHARACTERISTICS:

; LENGTH: 695 amino acids  
; TYPE: amino acid  
; STRANDEDNESS: single  
; TOPOLOGY: linear  
; MOLECULE TYPE: protein  
US-08-464-250-1

Query Match 99.5%; Score 3633; DB 3; Length 695;  
Best Local Similarity 99.7%; Pred. No. 1.1e-266;  
Matches 693; Conservative 1; Mismatches 1; Indels 0; Gaps 0;

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Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGTK 60
        |||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
        |||
Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
        |||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
        |||
Db    181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
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Db    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360
        |||
Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360

Qy    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
        |||
Db    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480
        |||
Db    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480

Qy    481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540
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Qy    541 DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600
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Qy    601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660
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Db    601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660

Qy    661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QN 695
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Db            661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695

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Job time : 16 secs

OM protein - protein search, using sw model

Run on: July 26, 2004, 12:40:23 ; Search time 13.6667 Seconds  
(without alignments)  
4905.768 Million cell updates/sec

Title: US-09-806-194A-18  
Perfect score: 3651  
Sequence: 1 MLPGLALLLLAAWTARALEV.....QQNGYENPTYKFFEQMQNKK 697

Scoring table: BLOSUM62  
Gapop 10.0 , Gapext 0.5

Searched: 283366 seqs, 96191526 residues

Total number of hits satisfying chosen parameters: 283366

Minimum DB seq length: 0  
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%  
Maximum Match 100%  
Listing first 45 summaries

Database : PIR\_78:\*  
1: pir1:\*  
2: pir2:\*  
3: pir3:\*  
4: pir4:\*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

# SUMMARIES

Result No.	% Query		Length	DB	ID	Description
	Score	Match				
1	3633	99.5	695	1	A49795	Alzheimer's diseas
2	3582.5	98.1	770	1	QRHUA4	Alzheimer's diseas
3	3536	96.9	695	2	S00550	Alzheimer's diseas
4	3511	96.2	695	2	A27485	Alzheimer's diseas
5	3095	84.8	747	2	JH0773	Alzheimer's diseas
6	2105	57.7	484	4	A32761	hypothetical Alzhe
7	1725	47.2	763	2	A49321	amyloid beta (A4)
8	1709	46.8	765	2	S42880	amyloid precursor-
9	1699	46.5	751	2	A49974	beta-amyloid precu
10	1183	32.4	653	2	A46362	amyloid precursor-
11	1138	31.2	511	2	JC1404	CDEI-box DNA-bindi
12	815.5	22.3	686	2	T15795	hypothetical prote
13	746	20.4	886	2	A32758	beta-amyloid-like

14	706	19.3	246	2	S38344	CDEI-binding prote
15	403	11.0	82	2	PQ0438	Alzheimer's diseas
16	289.5	7.9	191	2	A35981	sperm membrane pro
17	275	7.5	57	2	E60045	Alzheimer's diseas
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19	275	7.5	57	2	G60045	Alzheimer's diseas
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23	217	5.9	42	2	PN0512	beta-amyloid prote
24	192.5	5.3	1110	2	I51116	NF-180 - sea lampr
25	186	5.1	5170	2	T15348	hypothetical prote
26	185.5	5.1	407	1	EDBEQ3	immediate-early pr
27	185.5	5.1	993	2	S49461	synaptonemal compl
28	182	5.0	522	2	T32444	hypothetical prote
29	175.5	4.8	802	1	S48529	NAB3 protein - yea
30	175.5	4.8	1188	2	T46608	zinc finger protei
31	174	4.8	579	2	JH0820	160K golgi antigen
32	174	4.8	1087	2	T30330	gelsolin-related p
33	172	4.7	675	2	T03744	myoD protein inhib
34	172	4.7	784	2	PN0009	neurofilament trip
35	172	4.7	1182	2	T30189	myelin transcripti
36	171.5	4.7	793	1	JH0628	caldesmon - human
37	171.5	4.7	884	2	T20405	hypothetical prote
38	171.5	4.7	885	2	G71608	ATP-dept. acyl-CoA
39	171	4.7	1271	2	A45555	glutamate rich pro
40	170	4.7	464	2	H90279	microtubule bindin
41	170	4.7	1948	2	S00485	gene 11-1 protein
42	169.5	4.6	298	1	TPHUTC	troponin T, cardia
43	169.5	4.6	1875	2	S38173	myosin-like protei
44	169	4.6	771	1	A33430	h-caldesmon - chic
45	169	4.6	1187	2	T46637	transcription fact

# ALIGNMENTS

## RESULT 1

A49795

Alzheimer's disease amyloid beta protein precursor - crab-eating macaque

C;Species: *Macaca fascicularis* (crab-eating macaque)

C;Date: 10-Sep-1999 #sequence\_revision 10-Sep-1999 #text\_change 10-Sep-1999

C;Accession: A49795

R;Podlisny, M.B.; Tolan, D.R.; Selkoe, D.J.

Am. J. Pathol. 138, 1423-1435, 1991

A;Title: Homology of the amyloid beta protein precursor in monkey and human supports a primate model for beta amyloidosis in Alzheimer's disease.

A;Reference number: A49795; MUID:91273117; PMID:1905108

A;Accession: A49795

A;Status: preliminary

A;Molecule type: mRNA

A;Residues: 1-695 <POD>

A;Cross-references: GB:M58727; NID:g342062; PIDN:AAA36829.1; PID:g342063

C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology

C;Keywords: alternative splicing



Query Match 99.5%; Score 3633; DB 1; Length 695;  
Best Local Similarity 99.7%; Pred. No. 1.5e-183;  
Matches 693; Conservative 1; Mismatches 1; Indels 0; Gaps 0;

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Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

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Qy    361 QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
      |||
Db    361 QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA 480
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Db    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA 480

Qy    481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540
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Db    481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540

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      |||
Db    601 RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMMLKKKQYTSIHHGV 660

Qy    661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695
      |||
Db    661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695
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RESULT 2

QRHUA4

Alzheimer's disease amyloid beta protein precursor [validated] - human

N;Alternate names: Alzheimer's disease amyloid A4 protein; coagulation factor XIa inhibitor; proteinase nexin II (PN-II)

N;Contains: amyloid beta protein long, plaque form; amyloid beta protein short, vascular form; amyloid protein precursor splice form APP(695); amyloid protein precursor splice form APP(751); amyloid protein precursor splice form APP(770)

C;Species: Homo sapiens (man)

C;Date: 30-Jun-1987 #sequence\_revision 28-Jul-1995 #text\_change 15-Sep-2000

C;Accession: S02260; S05194; A32277; A33260; A35486; I39452; I39451; I39453; I59562; A44017; B44017; A03134; A29030; A47584; A47585; S02638; S00707; S00925; A38949; A30320; B30320; C30320; A31087; A24668; A28583; A29302; A60805; JL0038; S06121; A60355; A59011; A38384; S29076; S38252; S32539; S48148; S48692; S51186; S51185; S51184; S51183; A54238; I58075; I52250; S09010; S10737; S24127; S43644

R;Lemaire, H.G.; Salbaum, J.M.; Multhaup, G.; Kang, J.; Bayney, R.M.; Unterbeck, A.; Beyreuther, K.; Mueller-Hill, B.

Nucleic Acids Res. 17, 517-522, 1989

A;Title: The PreA4(695) precursor protein of Alzheimer's disease A4 amyloid is encoded by 16 exons.

A;Reference number: S02260; MUID:89128427; PMID:2783775

A;Accession: S02260

A;Molecule type: DNA

A;Residues: 1-288, 'V', 365-770 <LEM1>

A;Cross-references: EMBL:X13466

A;Note: alternative splice form APP(695)

R;Lemaire, H.G.

submitted to the EMBL Data Library, November 1988

A;Reference number: S05194

A;Accession: S05194

A;Molecule type: DNA

A;Residues: 1-14, 'VW', 17-288, 'V', 365-770 <LEM2>

A;Cross-references: EMBL:X13466; NID:g35598; PIDN:CAA31830.1; PID:g871360

A;Note: alternative splice form APP(695)

R;La Fauci, G.; Lahiri, D.K.; Salton, S.R.J.; Robakis, N.K.

Biochem. Biophys. Res. Commun. 159, 297-304, 1989

A;Title: Characterization of the 5'-end region and the first two exons of the beta-protein precursor gene.

A;Reference number: A32277; MUID:89165870; PMID:2538123

A;Accession: A32277

A;Molecule type: DNA

A;Residues: 1-75 <LAF>

A;Cross-references: GB:M24546; GB:M24547; NID:g341202; PIDN:AAC13654.1; PID:g516074

R;Johnstone, E.M.; Chaney, M.O.; Moore, R.E.; Ward, K.E.; Norris, F.H.; Little, S.P.

Biochem. Biophys. Res. Commun. 163, 1248-1255, 1989

A;Title: Alzheimer's disease amyloid peptide is encoded by two exons and shows similarity to soybean trypsin inhibitor.

A;Reference number: A33260; MUID:89392030; PMID:2675837

A;Accession: A33260

A;Molecule type: DNA

A;Residues: 656-737 <JOH>

A;Cross-references: GB:M29270; NID:gl78863; PIDN:AAA51768.1; PID:gl78865

R;Prelli, F.; Levy, E.; van Duinen, S.G.; Bots, G.T.A.M.; Luyendijk, W.; Frangione, B.

Biochem. Biophys. Res. Commun. 170, 301-307, 1990

A;Title: Expression of a normal and variant Alzheimer's beta-protein gene in amyloid of hereditary cerebral hemorrhage, Dutch type: DNA and protein diagnostic assays.

A;Reference number: A35486; MUID:90321244; PMID:2196878  
 A;Accession: A35486  
 A;Molecule type: DNA  
 A;Residues: 672-710 <PRE1>  
 A;Note: 693-Gln was found in DNA isolated from HCHWA-D patients  
 R;Yoshikai, S.I.; Sasaki, H.; Doh-ura, K.; Furuya, H.; Sakaki, Y.  
 Gene 87, 257-263, 1990  
 A;Title: Genomic organization of the human amyloid beta-protein precursor gene.  
 A;Reference number: I39451; MUID:90236318; PMID:2110105  
 A;Accession: I39452  
 A;Status: nucleic acid sequence not shown; translation not shown; translated  
 from GB/EMBL/DDBJ  
 A;Molecule type: DNA  
 A;Residues: 1-770 <YOS1>  
 A;Cross-references: GB:M33112; NID:g178613; PIDN:AAB59502.1; PID:g178616  
 A;Accession: I39451  
 A;Status: nucleic acid sequence not shown; translation not shown; translated  
 from GB/EMBL/DDBJ  
 A;Molecule type: DNA  
 A;Residues: 1-530, 'QWLMPVIPAFWEAKVGR' <YOS2>  
 A;Cross-references: GB:M34875; NID:g178608; PIDN:AAB59501.1; PID:g178615  
 R;Yoshikai, S.I.; Sasaki, H.; Doh-ura, K.; Furuya, H.; Sakaki, Y.  
 Gene 102, 291-292, 1991  
 A;Reference number: A59020; MUID:91340168; PMID:1908403  
 A;Contents: annotation; erratum  
 A;Note: revised physical map for reference I39451  
 R;Levy, E.; Carman, M.D.; Fernandez-Madrid, I.J.; Power, M.D.; Lieberburg, I.;  
 van Duinen, S.G.; Bots, G.T.; Luyendijk, W.; Frangione, B.  
 Science 248, 1124-1126, 1990  
 A;Title: Mutation of the Alzheimer's disease amyloid gene in hereditary cerebral  
 hemorrhage, Dutch type.  
 A;Reference number: I39453; MUID:90260663; PMID:2111584  
 A;Accession: I39453  
 A;Status: translated from GB/EMBL/DDBJ  
 A;Molecule type: DNA  
 A;Residues: 656-737 <LEV>  
 A;Cross-references: GB:M37896; NID:g178618; PIDN:AAA51727.1; PID:g178620  
 A;Note: a mutation with 693-Gln is presented  
 R;Murrell, J.; Farlow, M.; Ghetti, B.; Benson, M.D.  
 Science 254, 97-99, 1991  
 A;Title: A mutation in the amyloid precursor protein associated with hereditary  
 Alzheimer's disease.  
 A;Reference number: I59562; MUID:92022553; PMID:1925564  
 A;Accession: I59562  
 A;Status: translated from GB/EMBL/DDBJ  
 A;Molecule type: DNA  
 A;Residues: 689-716, 'F', 718-737 <MUR>  
 A;Cross-references: GB:S57665; NID:g236720; PIDN:AAB19991.1; PID:g236721  
 R;Kamino, K.; Orr, H.T.; Payami, H.; Wijsman, E.M.; Alonso, M.E.; Pulst, S.M.;  
 Anderson, L.; O'dahl, S.; Nemens, E.; White, J.A.; Sadovnick, A.D.; Ball, M.J.;  
 Kaye, J.; Warren, A.; McInnis, M.; Antonarakis, S.E.; Korenberg, J.R.; Sharma,  
 V.; Kukull, W.; Larson, E.; Heston, L.L.; Martin, G.M.; Bird, T.D.;  
 Schellenberg, G.D.  
 Am. J. Hum. Genet. 51, 998-1014, 1992  
 A;Title: Linkage and mutational analysis of familial Alzheimer disease kindreds  
 for the APP gene region.  
 A;Reference number: A44017; MUID:93035397; PMID:1415269

A;Accession: A44017  
 A;Molecule type: DNA  
 A;Residues: 687-692, 'G', 694-718 <KAM1>  
 A;Cross-references: GB:S45135; NID:g257377; PIDN:AAB23645.1; PID:g257378  
 A;Experimental source: familial Alzheimer disease family SB  
 A;Note: sequence extracted from NCBI backbone (NCBIP:115374)  
 A;Accession: B44017  
 A;Molecule type: DNA  
 A;Residues: 687-718 <KAM2>  
 A;Cross-references: GB:S45136; NID:g257379; PIDN:AAB23646.1; PID:g257380  
 A;Experimental source: familial Alzheimer disease family LIT  
 A;Note: sequence extracted from NCBI backbone (NCBIP:115376)  
 A;Note: this sequence has a silent mutation  
 R;Kang, J.; Lemaire, H.G.; Unterbeck, A.; Salbaum, J.M.; Masters, C.L.;  
 Grzeschik, K.H.; Multhaup, G.; Beyreuther, K.; Muller-Hill, B.  
 Nature 325, 733-736, 1987  
 A;Title: The precursor of Alzheimer's disease amyloid A4 protein resembles a  
 cell-surface receptor.  
 A;Reference number: A03134; MUID:87144572; PMID:2881207  
 A;Accession: A03134  
 A;Molecule type: mRNA  
 A;Residues: 1-288, 'V', 365-770 <KAN>  
 A;Cross-references: GB:Y00264; NID:g28525; PIDN:CAA68374.1; PID:g28526  
 A;Note: alternative splice form APP(695)  
 R;Robakis, N.K.; Ramakrishna, N.; Wolfe, G.; Wisniewski, H.M.  
 Proc. Natl. Acad. Sci. U.S.A. 84, 4190-4194, 1987  
 A;Title: Molecular cloning and characterization of a cDNA encoding the  
 cerebrovascular and the neuritic plaque amyloid peptides.  
 A;Reference number: A29030; MUID:87231971; PMID:3035574  
 A;Accession: A29030  
 A;Molecule type: mRNA  
 A;Residues: 284-288, 'V', 365-646, 'E', 648-770 <ROB>  
 A;Cross-references: GB:M16765; NID:g178539; PIDN:AAA51722.1; PID:g178540  
 A;Note: the authors translated the codon GAG for residue 647 as Asp  
 R;Goldgaber, D.; Lerman, M.I.; McBride, O.W.; Saffiotti, U.; Gajdusek, D.C.  
 Science 235, 877-880, 1987  
 A;Title: Characterization and chromosomal localization of a cDNA encoding brain  
 amyloid of Alzheimer's disease.  
 A;Reference number: A47584; MUID:87120328; PMID:3810169  
 A;Accession: A47584  
 A;Molecule type: mRNA  
 A;Residues: 674-756, 'S', 758-770 <GOL>  
 A;Cross-references: GB:M15533; NID:g178706; PIDN:AAA35540.1; PID:g178707  
 A;Experimental source: brain  
 R;Tanzi, R.E.; Gusella, J.F.; Watkins, P.C.; Bruns, G.A.P.; St George-Hyslop,  
 P.; Van Keuren, M.L.; Patterson, D.; Pagan, S.; Kurnit, D.M.; Neve, R.L.  
 Science 235, 880-884, 1987  
 A;Title: Amyloid beta protein gene: cDNA, mRNA distribution, and genetic linkage  
 near the Alzheimer locus.  
 A;Reference number: A47585; MUID:87120329; PMID:2949367  
 A;Accession: A47585  
 A;Molecule type: mRNA  
 A;Residues: 674-703 <TAN1>  
 A;Cross-references: GB:M15532; NID:g177957; PIDN:AAA51564.1; PID:g177958  
 R;Dyrks, T.; Weidemann, A.; Multhaup, G.; Salbaum, J.M.; Lemaire, H.G.; Kang,  
 J.; Mueller-Hill, B.; Masters, C.L.; Beyreuther, K.  
 EMBO J. 7, 949-957, 1988

A;Title: Identification, transmembrane orientation and biogenesis of the amyloid A4 precursor of Alzheimer's disease.  
 A;Reference number: S02638; MUID:88296437; PMID:2900137  
 A;Accession: S02638  
 A;Molecule type: mRNA  
 A;Residues: 672-678 <DYR>  
 R;Tanzi, R.E.; McClatchey, A.I.; Lamperti, E.D.; Villa-Komaroff, L.; Gusella, J.F.; Neve, R.L.  
 Nature 331, 528-530, 1988  
 A;Title: Protease inhibitor domain encoded by an amyloid protein precursor mRNA associated with Alzheimer's disease.  
 A;Reference number: S00707; MUID:88122640; PMID:2893290  
 A;Accession: S00707  
 A;Molecule type: mRNA  
 A;Residues: 286-344, 'I', 365-366 <TAN2>  
 A;Cross-references: EMBL:X06982; NID:g28817; PIDN:CAA30042.1; PID:g929612  
 A;Experimental source: promyelocytic leukemia cell line HL60  
 A;Note: alternative splice form APP(751)  
 R;Ponte, P.; Gonzalez-DeWhitt, P.; Schilling, J.; Miller, J.; Hsu, D.; Greenberg, B.; Davis, K.; Wallace, W.; Lieberburg, I.; Fuller, F.; Cordell, B.  
 Nature 331, 525-527, 1988  
 A;Title: A new A4 amyloid mRNA contains a domain homologous to serine proteinase inhibitors.  
 A;Reference number: S00925; MUID:88122639; PMID:2893289  
 A;Accession: S00925  
 A;Molecule type: mRNA  
 A;Residues: 1-344, 'I', 365-770 <PO2>  
 A;Cross-references: GB:X06989; EMBL:Y00297; NID:g28720; PIDN:CAA30050.1; PID:g28721  
 A;Note: alternative splice form APP(751)  
 R;Kitaguchi, N.; Takahashi, Y.; Tokushima, Y.; Shiojiri, S.; Ito, H.  
 Nature 331, 530-532, 1988  
 A;Title: Novel precursor of Alzheimer's disease amyloid protein shows protease inhibitory activity.  
 A;Reference number: A38949; MUID:88122641; PMID:2893291  
 A;Accession: A38949  
 A;Molecule type: mRNA  
 A;Residues: 287-367 <KIT>  
 A;Cross-references: GB:X06981; NID:g28816; PIDN:CAA30041.1; PID:g929611  
 A;Experimental source: glioblastoma cell line  
 A;Note: alternative splice form APP(770)  
 R;Vitek, M.P.; Rasool, C.G.; de Sauvage, F.; Vitek, S.M.; Bartus, R.T.; Beer, B.; Ashton, R.A.; Macq, A.F.; Maloteaux, J.M.; Blume, A.J.; Octave, J.N.  
 Brain Res. Mol. Brain Res. 4, 121-131, 1988  
 A;Title: Absence of mutation in the beta-amyloid cDNAs cloned from the brains of three patients with sporadic Alzheimer's disease.  
 A;Reference number: A30320  
 A;Accession: A30320  
 A;Status: not compared with conceptual translation  
 A;Molecule type: mRNA  
 A;Residues: 284-288, 'V', 365-770 <VIT1>  
 A;Accession: B30320  
 A;Status: not compared with conceptual translation  
 A;Molecule type: mRNA  
 A;Residues: 122-288, 'V', 365-770 <VIT2>  
 A;Accession: C30320  
 A;Status: not compared with conceptual translation

A;Molecule type: mRNA  
A;Residues: 606-770 <VIT3>  
R;Zain, S.B.; Salim, M.; Chou, W.G.; Sajdel-Sulkowska, E.M.; Majocha, R.E.; Marotta, C.A.  
Proc. Natl. Acad. Sci. U.S.A. 85, 929-933, 1988  
A;Title: Molecular cloning of amyloid cDNA derived from mRNA of the Alzheimer disease brain: coding and noncoding regions of the fetal precursor mRNA are expressed in the cortex.  
A;Reference number: A31087; MUID:88124954; PMID:2893379  
A;Accession: A31087  
A;Molecule type: mRNA  
A;Residues: 507-770 <ZAI>  
A;Cross-references: GB:M18734; NID:g178572; PIDN:AAA51726.1; PID:g178573  
A;Note: the authors translated the codon GAA for residue 599 as Gly, ACC for residue 603 as Val, GTG for residue 604 as Glu, GAG for residue 605 as Leu, CTT for residue 607 as Pro, CCC for residue 608 as Val, GTG for residue 609 as Asn, AAT for residue 610 as Gly, and GGT for residue 655 as Ser  
A;Note: the cited Genbank accession number, J03594, is not in release 101.0  
R;Masters, C.L.; Multhaup, G.; Simms, G.; Pottgiesser, J.; Martins, R.N.; Beyreuther, K.

Query Match 98.1%; Score 3582.5; DB 1; Length 770;  
Best Local Similarity 89.9%; Pred. No. 7.8e-181;  
Matches 692; Conservative 2; Mismatches 1; Indels 75; Gaps 1;

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Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
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Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
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Qy    181 GVEFVCCPLAEESDNVDSADAEEDDSVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE 240
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Db    181 GVEFVCCPLAEESDNVDSADAEEDDSVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE 240

Qy    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVR----- 288
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Db    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVREVCSEQAETGPC 300

Qy    289 ----- 288

Db    301 RAMISRWFYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMVCGSAMSQSLLKTTQEPLARD 360

Qy    289 ---VPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQA 345
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Db    361 PVKLPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQA 420

Qy    346 KNLPKADKKAVIQHFQEKVESLEQEANERQQLVETHMARVEAMLNDRRRLALENYITAL 405
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Qy 406 QAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYER 465  
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 Db 481 QAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYER 540  
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 Qy 466 MNQSLSLLYNVPAAVEEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDALMPSLTET 525  
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 Db 541 MNQSLSLLYNVPAAVEEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDALMPSLTET 600  
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 Qy 526 KTTVELLPVNGEFSLDDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTN 585  
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 Db 601 KTTVELLPVNGEFSLDDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTN 660  
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 Qy 586 IKTEEISEVNLDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITL 645  
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 Db 721 VMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 770  
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# RESULT 3

S00550

Alzheimer's disease amyloid beta protein precursor - rat

N;Alternate names: beta-A4 amyloid protein

C;Species: Rattus norvegicus (Norway rat)

C;Date: 30-Jun-1989 #sequence\_revision 30-Jun-1989 #text\_change 13-Aug-1999

C;Accession: S00550; A41245; A39820; S46251

R;Shivers, B.D.; Hilbich, C.; Multhaup, G.; Salbaum, M.; Beyreuther, K.;

Seeburg, P.H.

EMBO J. 7, 1365-1370, 1988

A;Title: Alzheimer's disease amyloidogenic glycoprotein: expression pattern in rat brain suggests a role in cell contact.

A;Reference number: S00550; MUID:88312583; PMID:2900758

A;Accession: S00550

A;Molecule type: mRNA

A;Residues: 1-695 <SHI>

A;Cross-references: EMBL:X07648; NID:g55616; PIDN:CAA30488.1; PID:g55617

R;Schubert, D.; Schroeder, R.; LaCorbiere, M.; Saitoh, T.; Cole, G.

Science 241, 223-226, 1988

A;Title: Amyloid beta protein precursor is possibly a heparan sulfate proteoglycan core protein.

A;Reference number: A41245; MUID:88264430; PMID:2968652

A;Accession: A41245

A;Molecule type: protein

A;Residues: 18-37, 'X', 39-40, 'X', 42-44 <SCH>

A;Note: evidence for heparan sulfate attachment

R;Hesse, L.; Beher, D.; Masters, C.L.; Multhaup, G.

FEBS Lett. 349, 109-116, 1994

A;Title: The beta-A4 amyloid precursor protein binding to copper.

A;Reference number: S46251; MUID:94320627; PMID:7913895

A;Contents: annotation; copper binding sites

A;Note: rat peptides were isolated but not sequenced

R;Potempska, A.; Styles, J.; Mehta, P.; Kim, K.S.; Miller, D.L.

J. Biol. Chem. 266, 8464-8469, 1991

A;Title: Purification and tissue level of the beta-amyloid peptide precursor of rat brain.

A;Reference number: A39820; MUID:91217087; PMID:1673681  
A;Accession: A39820  
A;Status: preliminary  
A;Molecule type: protein  
A;Residues: 18-32 <POT>  
A;Experimental source: brain  
C;Comment: Deposition of amyloid protein as neurofibrillary tangles and/or plaques is characteristic of both Alzheimer's disease and Down's syndrome.  
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology  
C;Keywords: alternative splicing; amyloid; glycoprotein; transmembrane protein  
F;625-648/Domain: transmembrane #status predicted <TMM>

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Matches 674; Conservative 8; Mismatches 13; Indels 0; Gaps 0;

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Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG		120
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Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR		180
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Qy	241	EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV		300
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Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA		480
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Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL		540
Db	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL		540
Qy	541	DDLQPWHSFGADSVPAANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVNDAEF		600
Db	541	DDLQPWHPFGVDSVPANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF		600







A;Title: A Xenopus homologue of the human beta-amyloid precursor protein: developmental regulation of its gene expression.  
A;Reference number: JH0773; MUID:93129227; PMID:1282805  
A;Accession: JH0773  
A;Molecule type: mRNA  
A;Residues: 1-747 <OKA>  
A;Cross-references: GB:S52417; NID:g263150; PIDN:AAB24853.1; PID:g263151  
A;Experimental source: larva  
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology  
C;Keywords: alternative splicing; amyloid  
F;287-337/Domain: animal Kunitz-type proteinase inhibitor homology <BPI>

Query Match 84.8%; Score 3095; DB 2; Length 747;  
Best Local Similarity 80.8%; Pred. No. 3e-155;  
Matches 596; Conservative 36; Mismatches 42; Indels 64; Gaps 5;

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Qy      17 ALEVPTDGNAGLLAEPQIAMF-CGRLNMHMNVQNGKWSDPSGKTCTCIDTKEGILQYCQE 75
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Db      15 ALEVLVDGNGGLLAEPQIAMFSVARLNMHMNVQNGKWETDVSG---CIGTKEGILQYCQE 71

Qy      76 VYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVGEFVSDALLVPDKCKF 135
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Db      72 VYPELQITNVVEANQPVTIQNWCKKGRKQCKSRTHIVVPYRCLVGEFVSDALLVPDKCKF 131

Qy     136 LHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFRGVEFVCCPLAEESDN 195
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Qy     196 VDSADAEEDSDVWVGADTDYADGSEDKVVEVA--EEEEVAEVEEEEADDDDEDDEDGDE 253
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Qy     254 VEEEAEEPVEEATERTTSIATTTTTTTTSEVEEVVR----- 288
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Db     250 AEEPEEPVEEATERTTSIATTTTTTTTSEVEEVREVCSEQAETGPCRAMISRWYYDVTE 309

Qy     289 -----VPTTAASTPDAVDKYLETPGDENEHAHFQ 317
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Qy     318 KAKERLEAKHRERMSQVMREWEAERQAKNLPKADKKAVIQHFQEKVESLEQEAAANERQQ 377
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Db     370 KAKERLEGKHREKMSEVMKEWEAERQAKNLPKADKKAVIQHFQEKVESLEQEAAKQRQQ 429

Qy     378 LVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHF 437
      ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db     430 LVETHMARVEAMLNDRRRIALENYITALQADPPRPRHVFNMLKKYVRAEQKDRQHTLKHF 489

Qy     438 EHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAVAEEIQDEVDELLQKEQNY 497
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Db     490 EHVRMVDPKKAAQIRSQVMTHLRVINERMNQSFSLLYKVPVAVAEEIQDEVDELQKEQNY 549

Qy     498 SDDVLANMISEPRI SYGNDALMPSLTETKTTVELLPVNGEFLDDLQPWHSFGADSVPAN 557
      |||::|||::| :||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db     550 SDDMVSNMVS DHRVSYGNDALMPSLSETKTTVELLPVDGEFNIEDLQPWHSFGVDSVPAN 609

```

```

Qy      558 TENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLDAEFRHDSGYEVHHQKLVFFA 617
          |||
Db      610 TENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDSEYRHDTAYEVHHQKLVFFA 669

Qy      618 EDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGVVEVDAAVTPEERHLSKM 677
          |:|
Db      670 EEVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTTIHGGVVEVDAAVTPEERHLTKM 729

Qy      678 QQNGYENPTYKFFEQMQN 695
          |||
Db      730 QQNGYENPTYKFFEQMQN 747

```

# RESULT 6

A32761

hypothetical Alzheimer's disease amyloid beta protein, Alu-containing clone - human (fragment)

C;Species: Homo sapiens (man)

C;Date: 29-Jan-1990 #sequence\_revision 10-Apr-1996 #text\_change 10-Apr-1996

C;Accession: A32761

R;de Sauvage, F.; Octave, J.N.

Science 245, 651-653, 1989

A;Title: A novel mRNA of the A4 amyloid precursor gene coding for a possibly secreted protein.

A;Reference number: A32761; MUID:89346754; PMID:2569763

A;Accession: A32761

A;Molecule type: mRNA

A;Residues: 1-484 <DES>

A;Cross-references: GB:M28373

A;Note: the authors translated the codon ATG for residue 433 as Leu

C;Comment: This is the hypothetical translation of a sequence believed to contain cloning artifacts.

C;Keywords: cloning artifact

```

Query Match          57.7%;  Score 2105;  DB 4;  Length 484;
Best Local Similarity 87.7%;  Pred. No. 1.8e-103;
Matches 407;  Conservative 1;  Mismatches 0;  Indels 56;  Gaps 1;

```

```

Qy      80 LQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVGEFVSDALLVPDKCKFLHQE 139
          |||
Db      1  LQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVGEFVSDALLVPDKCKFLHQE 60

Qy     140 RMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFRGVEFVCCPLAEESDNVDSA 199
          |||
Db      61 RMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFRGVEFVCCPLAEESDNVDSA 120

Qy     200 DAEEDDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEEADDDDEDGDEVEEEEAE 259
          |||
Db     121 DAEEDDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEEADDDDEDGDEVEEEEAE 180

Qy     260 EPYEEATERTTSIATTTTTTTTESVEEVVR----- 288
          |||
Db     181 EPYEEATERTTSIATTTTTTTTESVEEVVREVCSEAETGPCRAMISRWFYDVTGKCAPF 240

Qy     289 -----VPTTAASTPDAVDKYLETPGDENEHAHFQKAKERL 323
          :|||
Db     241 FYGGCGGNRNNFDTEEYCMVCGSAIPTTAASTPDAVDKYLETPGDENEHAHFQKAKERL 300

```

Qy 324 EAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHFQEKVESLEQEAAANERQQLVETHM 383  
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||  
 Db 301 EAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHFQEKVESLEQEAAANERQQLVETHM 360

Qy 384 ARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMV 443  
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||  
 Db 361 ARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMV 420

Qy 444 DPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAAVEEIQDEV 487  
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||  
 Db 421 DPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAAVEEIQDEV 464

# RESULT 7

A49321

amyloid beta (A4) homolog 2 precursor - human

N;Alternate names: CDEI-binding protein

C;Species: Homo sapiens (man)

C;Date: 24-Feb-1994 #sequence\_revision 18-Nov-1994 #text\_change 13-Aug-1999

C;Accession: A49321; S34644; S40519

R;Sprecher, C.A.; Grant, F.J.; Grimm, G.; O'Hara, P.J.; Norris, F.; Norris, K.; Foster, D.C.

Biochemistry 32, 4481-4486, 1993

A;Title: Molecular cloning of the cDNA for a human amyloid precursor protein homolog: evidence for a multigene family.

A;Reference number: A49321; MUID:93250009; PMID:8485127

A;Accession: A49321

A;Status: preliminary

A;Molecule type: mRNA

A;Residues: 1-763 <SPR>

A;Cross-references: GB:S60099; NID:g300168; PIDN:AAC60589.1; PID:g300169

A;Experimental source: placenta

A;Note: sequence extracted from NCBI backbone (NCBIN:131198, NCBI:P:131199)

A;Note: expression was shown in placenta, brain, heart, lung, liver, and kidney

R;von der Kammer, H.; Klaudiny, J.; Hanes, J.; Scheit, K.H.

submitted to the EMBL Data Library, April 1993

A;Description: The human homologue of the murine CDEI binding protein is an amyloid precursor like protein.

A;Reference number: S34644

A;Accession: S34644

A;Molecule type: mRNA

A;Residues: 1-763 <VON>

A;Cross-references: EMBL:Z22572; NID:g394763; PIDN:CAA80295.1; PID:g394764

R;Wasco, W.; Gurubhagavatula, S.; Paradis, M.; Romano, D.M.; Sisodia, S.S.;

Hyman, B.T.; Neve, R.L.; Tanzi, R.E.

Nature Genet. 5, 95-99, 1993

A;Title: Isolation and characterization of APLP2 encoding a homologue of the Alzheimer's associated amyloid beta protein precursor.

A;Reference number: S40519; MUID:94035131; PMID:8220435

A;Accession: S40519

A;Status: preliminary

A;Molecule type: mRNA

A;Residues: 1-763 <WAS>

A;Cross-references: GB:L27631; NID:g450391; PIDN:AAC41701.1; PID:g450392

C;Genetics:

A;Gene: GDB:APLP2; APPL2

A;Cross-references: GDB:139159; OMIM:104776

A;Map position: 11q23-11q25

C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology

C;Keywords: alternative splicing; transmembrane protein

F;310-360/Domain: animal Kunitz-type proteinase inhibitor homology <BPI>

Query Match 47.2%; Score 1725; DB 2; Length 763;  
Best Local Similarity 46.9%; Pred. No. 2.9e-83;  
Matches 369; Conservative 112; Mismatches 170; Indels 136; Gaps 19;

```
Qy      5 LALLLLAAWTARALEV-----PTDGNAG---LLAEPQIAMFCGRLNMHNMNVQNGKWDSDP 56
      | | | | | | | | : | | | | | | | | | | | | | | | | | | | | | | |
Db     15 LLLLLLVGLTAPALALAGYIEALAANAGTGFVAEAPQIAMFCGKLNMHVNIQTGKWEPPD 74

Qy     57 SGTKTCTIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYR 116
      : | | | : | | | : | | | | | | | | | | | | | | | | | | | | | | |
Db     75 TGTKSCFETKEEVLYCQEMYPELQITNVMEANQVRSIDNWCRRDKKQCKS--RFVTPFK 132

Qy    117 CLVGEFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGI 176
      | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
Db    133 CLVGEFVSDVLLVPEKQOFFHKERMEVCENHQHWHTVVKEACLTQGMTLYSYGMLLPCGV 192

Qy    177 DKFRGVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAE 236
      | : | | | | | | : : | : | | : : | | | | : | | | :
Db    193 DQFHGTEYVCCPQTKIIGSVSKEEEEEDEE-----EEEEDEEEDYDVYKSEFPTEAD 245

Qy    237 VEE--EEA--DDDEDDDEDGDEVEEEAEOPY-----EEATERTTSIATTTTTTTTES 282
      : | : | | | | | | | | | | | | | | | | | | | | | | | |
Db    246 LEDFTEAAVDEDEDEEEGEEVVEDRDYYDTFKGDDYNEENPTEPGSDGTMSDKEITHD 305

Qy    283 VEEV-----VRVP 290
      | : | | | | | | | | | | | | | | | | | | | | | | | |
Db    306 VKAVCSQEAMTGPCRAVMPRWYFDLSKGKCVRFIYGGCGGNRNFESEDYCMVCKAMIP 365

Qy    291 TTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPK 350
      | | | | | | | | | | | | | | | | | | | | | | | | | |
Db    366 PTPLPTND-VDVYFETSADDNEHARFQKAKEQLEIRHRNRMDRVKKEWEEAELQAKNLPK 424

Qy    351 ADKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPP 410
      | : : : | | | | | | | | | | | | | | | | | | | | | | | |
Db    425 AERQTLIQHFQAMVKALEKEAASEKQQLVETHLARVEAMLNDRRRMALENYLAALQSDPP 484

Qy    411 RPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQL 470
      | | : | : | | | | | | | | | | | | | | | | | | | | |
Db    485 RPHRILQALRRYVRAENKDRDLHTIRHYQHVLAVDPEKAAQMKSQVMTHLVIEERNQL 544

Qy    471 SLLYNVPAVAEEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTVE 530
      | | | | | | | | | | | | | | | | | | | | | | | | | |
Db    545 SLLYKVPYVAQEIQEEIDELLQEQR-----ADM-----DQFTASISETPVDVR 587

Qy    531 LLPVNGEFSDDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPG-----SGLTN 585
      | : | | : : | : | | | | | | | | | | | | | | | | |
Db    588 ---VSSEES-EEIPPFHPP--HPFPALPENE---DTQPELYHPMKKSGVGEQDGGGLIG 637

Qy    586 IKTEEISEVN-LDAEFRHDSGYEVHHQKLVFFAEDVGS-----NKGAI 627
      : : | : | : | | : | : : | | | | | | | | | | | |
```

Db 638 AEEKVINSKNKVDENMVIDETLDV--KEMIFNAERVGGLEERESVGPLREDFSLSSAL 695

Qy 628 IGLMVGGVVIATVIVITLVMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTY 687  
 |||:| | |||||:||||:|:| | ||:|||| :|||||:||| :|||||

Db 696 IGLLVIAVAIATVIVISLVMLRKRQYGTISHGIVEVDPMLTPEERHLNKMQNHHGYENPTY 755

Qy 688 KFFEQQMQ 694  
 |: |||

Db 756 KYLEQQMQ 762

# RESULT 8

S42880

amyloid precursor-like protein - rat

C;Species: Rattus norvegicus (Norway rat)

C;Date: 06-Jan-1995 #sequence\_revision 06-Jan-1995 #text\_change 17-Mar-1999

C;Accession: S42880; S47528

R;Sandbrink, R.; Masters, C.L.; Beyreuther, K.

submitted to the EMBL Data Library, March 1994

A;Description: Complete nucleotide and deduced amino acid sequence of rat amyloid precursor-like protein 2 (Aplp2/Apph): Two amino acids length difference to human and murine homologues.

A;Reference number: S42880

A;Accession: S42880

A;Molecule type: mRNA

A;Residues: 1-765 <SAN>

A;Cross-references: EMBL:X77934

R;Sandbrink, R.; Masters, C.L.; Beyreuther, K.

Biochim. Biophys. Acta 1219, 167-170, 1994

A;Title: Complete nucleotide and deduced amino acid sequence of rat amyloid protein precursor-like protein 2 (APLP2/APPH): two amino acids length difference to human and murine homologues.

A;Reference number: S47528; MUID:94368849; PMID:8086458

A;Accession: S47528

A;Status: preliminary

A;Molecule type: mRNA

A;Residues: 1-765 <SA2>

A;Cross-references: EMBL:X77934

C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology

C;Keywords: alternative splicing

F;312-362/Domain: animal Kunitz-type proteinase inhibitor homology <BPI>

Query Match . 46.8%; Score 1709; DB 2; Length 765;

Best Local Similarity 45.9%; Pred. No. 2e-82;

Matches 361; Conservative 124; Mismatches 168; Indels 134; Gaps 20;

Qy 5 LALLLLAAWTARALEV-----PTDGNAG---LLAEPQIAMFCGRLNMHMNVQNGKWDSDP 56  
 | :||| || | : ||| :|||||||:||||:| | ||: ||

Db 15 LLVLLLLGLTAPAAALAGYIEALAANAGTGFAVAEPQIAMFCGKLNMHVNIQTGKWEPPD 74

Qy 57 SGTKTCTIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYR 116  
 :|||:| | | :|||||:|||||||:||||| | :||:| :|||:| | |||:|

Db 75 TGTKSCLGTKEEVLQYCQEIYPQLQITNVMEANQPVNIDSWCRRDKKQCRS--HIVIPFK 132

Qy 117 CLVGEFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGI 176  
 ||||||| ||||: |:| |||||:||| | |||| || | : |: |||||||:







```

Qy      522 LTETKTTVELLPVNGEFLDDLPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGS 581
          : : |   | :   | :   | | |   | : : | |   | : : |
Db      579 ISENPVDVRVSSESE-EIPPFHPLHPF-----PSLSENE-----GSGMAEQDG- 621

Qy      582 GLTNIKTEEISEVN-LDAEFRHDSGYEVHHQKLVFFAEDVGS-----N 623
          || : : | : | : |   | : | : : : | | | |   :
Db      622 GLIGAEKVINSKNKMMDENMVIDETLDV--KEMIFNAERVGGLEEEPESVGPLREDFSL 679

Qy      624 KGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGVEVDAAVTPEERHLSKMQQNGYE 683
          | : | | : | | | | | | : | | | : | | : | | | | : | | |
Db      680 SNALIGLLVIAVAIATVIVISLVMLRKRQYGTISHGIVEVDPMLTPEERHLNKMQNHYGE 739

Qy      684 NPTYKFFEQMQ 694
          | | | | : | | |
Db      740 NPTYKYLEQMQ 750

```

# RESULT 10

A46362

amyloid precursor-like protein - mouse

C;Species: Mus musculus (house mouse)

C;Date: 21-Sep-1993 #sequence\_revision 18-Nov-1994 #text\_change 24-Nov-1999

C;Accession: A46362

R;Wasco, W.; Bupp, K.; Magendantz, M.; Gusella, J.F.; Tanzi, R.E.; Solomon, F.  
Proc. Natl. Acad. Sci. U.S.A. 89, 10758-10762, 1992

A;Title: Identification of a mouse brain cDNA that encodes a protein related to  
the Alzheimer disease-associated amyloid beta protein precursor.

A;Reference number: A46362; MUID:93066322; PMID:1279693

A;Accession: A46362

A;Status: preliminary

A;Molecule type: nucleic acid

A;Residues: 1-653 <WAS>

A;Experimental source: brain

A;Note: sequence inconsistent with the nucleotide translation

A;Note: sequence extracted from NCBI backbone (NCBIN:118683, NCBIP:118684)

C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type  
proteinase inhibitor homology

C;Keywords: transmembrane protein

```

Query Match          32.4%;  Score 1183;  DB 2;  Length 653;
Best Local Similarity 39.0%;  Pred. No. 7.1e-55;
Matches 275;  Conservative 121;  Mismatches 221;  Indels 88;  Gaps 20;

```

```

Qy      1 MLPGLALLLLAAWTARA-LEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGT 59
          : | | : | | | | | | | | : | | | | : | : : | : | : | :
Db      22 LLP-LSLLLLRAQLAVGNLAVGSPSAEAPGSAQVAGLCGRLTLHRDLRTGRWEPDPQRS 80

Qy      60 KTCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHF-VIPYRCL 118
          : | : : | : | : : | | | | | | : | : : | | | | | | | : | : |
Db      81 RRCLLDLPQRVLEYCRQMYPELHIARVEQAAQAI PMERWCGGTRSGRCAHPHHEVVPFHCL 140

Qy      119 VGEFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDK 178
          | | | | : | | | | : | : | | | | | | | | : | | | | | | | :
Db      141 PGEFVSEALLVPEGCRFLHQERMDQCESSTRRHQEAQAEACSSQGLILHGSGMLLPCGSDR 200

Qy      179 FRGVEFVCCPLAEESDNVDSADAEEDDSVDVW-WGGADTDYADGSEDKVVEVAEEEEVAEV 237
          | | | | : | | | : | : : | | | | : | | | | | | |

```

```

Db      201 FRGVEYVCCP-PPATPNPSGMAAGDPSTRSWPLGGR----AEGGED-----EEEVESF 248
Qy      238 EEEEADDDDEDEDGDEVEEEAEEPVEEATERTTSIATTTTTTTTESVEEVVRVPTTAASTP 297
      : | : :| ||| | : | : : | | ||
Db      249 PQPVDDYFVEPPQAEAAAAAAAAEERAPPPSSHTPVMVSRVTPTPR-----PT----- 294
Qy      298 DAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVI 357
      | | | | :| : || | :|| | : : :||| | :| :||| | :| :|
Db      295 DGVDVYFGMPGEIGEHEGFLRAKMDLEERRMRQINEVMREWAMADSQSKNLPKADRQALN 354
Qy      358 QHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFN 417
      :||| : :||| : : ||| :||| | | : :||| | | : | | | | : |
Db      355 EHFQSILQTLQVSGERQRLVETHATRVIALINDQRRAALEGFLAALQGDPPQAERVLM 414
Qy      418 MLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVP 477
      | : :| :||| : :||| :||| | | :| | | | :| | | | | | | | |
Db      415 ALRRYLRAEQKEQRHTLRHYQHVAVDPEKAQQMRQVQVQTHLQVIEERMNQSLSGLLDQNP 474
Qy      478 AVAEEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDALMP-SLTETKTTVELLPVNG 536
      :| :| : : ||| | | : : | | :| | :| |
Db      475 HLAQELRPQIQELL-----LAEHLGPSEL---DASVPGSSSEDK----- 510
Qy      537 EFSLDDLQPWHSFGADSVPANTENEVEPVDPARPAADRGLTTRPGSG-----LTNIKTEEI 591
      ||| | : :| | | :| | : | | :| :|
Db      511 ----GSLQP-----PESKDDPPVTLP---KGSTDQESSSSGREKLTPLEQYE- 550
Qy      592 SEVNLDAEFRHDSGYEVHH---QKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVML 648
      :|| | :| | : | :| :| :| :| :| :| :| :| :| :| :| :|
Db      551 QKVNASA----PRGFPHSSDIQRDELAPSGTGVSREALSGLLIMGAGGSLIVLSLLLL 606
Qy      649 -KKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQ 692
      ||| | :| ||||| :| ||| :| :| :| :| :| :| :| :|
Db      607 RKKKPYGTISHGVVEVDPMLTLEEQLRELQRHGYENPTYRFLEE 651

```

# RESULT 11

JC1404

CDEI-box DNA-binding protein - mouse

C;Species: Mus musculus (house mouse)

C;Date: 30-Sep-1993 #sequence\_revision 30-Sep-1993 #text\_change 16-Feb-1997

C;Accession: JC1404

R;Vidal, F.; Blangy, A.; Rassoulzadegan, M.; Cuzin, F.

Biochem. Biophys. Res. Commun. 189, 1336-1341, 1992

A;Title: A murine sequence-specific DNA binding protein shows extensive local similarities to the amyloid precursor protein.

A;Reference number: JC1404; MUID:93129193; PMID:1482349

A;Accession: JC1404

A;Molecule type: mRNA

A;Residues: 1-511 <VID>

C;Comment: This protein plays an important role in the early development of the mouse.

C;Keywords: DNA binding; transmembrane protein

Query Match 31.2%; Score 1138; DB 2; Length 511;

Best Local Similarity 45.4%; Pred. No. 1.2e-52;

Matches 251; Conservative 93; Mismatches 129; Indels 80; Gaps 16;



A;Experimental source: strain Bristol N2; clone C42D8  
R;Daigle, I.; Li, C.  
Proc. Natl. Acad. Sci. U.S.A. 90, 12045-12049, 1993  
A;Title: apl-1, a *Caenorhabditis elegans* gene encoding a protein related to the human beta-amyloid protein precursor.  
A;Reference number: A49414; MUID:94089766; PMID:8265668  
A;Accession: A49414  
A;Status: preliminary  
A;Molecule type: mRNA  
A;Residues: 7-686 <DAI>  
A;Cross-references: GB:U00240; NID:g416296; PIDN:AAC46470.1; PID:g416297  
C;Genetics:  
A;Gene: CESP:C42D8.8  
A;Map position: X  
A;Introns: 22/3; 78/3; 121/1; 199/1; 230/1; 274/3; 344/3; 410/2; 471/2; 537/3; 580/3  
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology

```

Db      415 RINGTLAMLRDFPDLEKYVRPIAVTYWKDYRDEVS PDISVE----DSELTPIIHDDEFSK 470
Qy      514 GN--DALMPSLT----ETKTTVELLPVNGEFLDDLQPWHSFGADSV PANT---ENEVEP 564
      |  | : |  :  : : |  | : :  :  |  | : : |
Db      471 NAKLDVKAPTTTAKPVKETDNAKVLPT EASDSEEEADEYYEDEDDEQVKKTPDMKKKVKV 530
Qy      565 VДАРP-----AADRGLTTRPGSGLTNIKTEE-----ISEVNLDA 598
      || : |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
Db      531 VDIKPKEIKVTIEEEKKAPKLVETSVQT DDEDDDEDSSSSTSSESEDEDEDKNIKELRVDI 590
Qy      599 E-----FRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLK 649
      |  : ||  || : |  |  |  |  |  |  |  |  |  |  |  |  |
Db      591 EPIIDEPASFYRHD-----KLIQSPEVERSASSVFQPYVLASAMFITAICIIAFAIT 642
Qy      650 KKQYTSIHGVEVDAAVTPEERHLSKMQQNGYENPTYKFFE 691
      :  | : ||  || || || : : || || || || || || :
Db      643 NARRRRAMRGFIEVD-VYTPEERHVAGMQVNGYENPTYSFDD 683

```

# RESULT 13

A32758

beta-amyloid-like protein precursor - fruit fly (*Drosophila melanogaster*)

C;Species: *Drosophila melanogaster*

C;Date: 08-Dec-1989 #sequence\_revision 08-Dec-1989 #text\_change 24-Sep-1998

C;Accession: A32758

R;Rosen, D.R.; Martin-Morris, L.; Luo, L.; White, K.

Proc. Natl. Acad. Sci. U.S.A. 86, 2478-2482, 1989

A;Title: A *Drosophila* gene encoding a protein resembling the human beta-amyloid protein precursor.

A;Reference number: A32758; MUID:89184650; PMID:2494667

A;Accession: A32758

A;Status: preliminary

A;Molecule type: mRNA

A;Residues: 1-886 <ROS>

A;Cross-references: GB:J04516; NID:g158371; PID:g158372

C;Genetics:

A;Gene: FlyBase:Appl

A;Cross-references: FlyBase:FBgn0000108

C;Keywords: transmembrane protein

Query Match 20.4%; Score 746; DB 2; Length 886;

Best Local Similarity 25.5%; Pred. No. 9.4e-32;

Matches 233; Conservative 126; Mismatches 289; Indels 264; Gaps 29;

```

Qy      7 LLLLAAWTARALEVPTDGNAGLLA-----EPQIAMFC--GRLNMHMNV-QNGKWDS DPSG 58
      ||| : |  | :  |  | : |  |||| : |  | :  :  : : | : |
Db      9 LLLRSLWVVLAI-----GTAQVQAASPRWEPQIAVLCEAGQIYQPQYLSEGRWVTDLSK 63
Qy      59 T---KTCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRG---RKQCKTHPHFV 112
      || : |  : | || : ||  ||| : || :  |  || : |  : ||  : :
Db      64 KTTGPTCLRDKMDLLDYCKKAYPNRDITNIVESSHYQKIGGWCRQGALNAAKCKGSHRWI 123
Qy      113 IPYRCLVGEFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLL 172
      | : || |  |  || || || : |  |  |  |  |  : :  |  | :  : |||
Db      124 KPFRCL-GPFQSDALLVPEGCLFDHIHNASRCWPFVRWNQTGAAACQERGMQMRTFAMLL 182
Qy      173 PCGIDKFRGVEFVCCP-----LAESDNVD---SA 199

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      |||| | |||||
Db      183 PCGISVFSGVFVCCPKHFKTDEIHVKKTDLVMPAAQINSANDELMNDEDDSDNSNYSK 242
Qy      200 DAEEDSDVWVGADTDYADGSEDKVVEVAEEEEV-----AEV 237
      || ||| | | | : : | : |
Db      243 DANEDDL-----DEDDLMDGDEEDDMVADEAATAGGSPNTGSSGDSNSGSLDDINA EY 296
Qy      238 EE-EEADDDDEDEDGDEVEEEAE EPY-----EEATERT 269
      : || | : | : | | | : | : | :
Db      297 DSGEEDNYEEDGAGSESEAEVEASWDQSGGAKVVSLSKSDSSSPSSAPVAPAPEKAPVKS 356
Qy      270 TSIATTTTTTTSVEEV-----RVPTTAASTPDAVDKYLETPGDENEHAHFQK 318
      | : : | : : | | : | | | | | : | :
Db      357 ESVTSTPQLSASAAAFVAANSNGSGTGAGAPPSTAQPTS---DPYFTHFDPHYEHQSYKV 413
Qy      319 AKERLEAKHRERMSQVMREWEAEERQAKNLPKADKKA-----VIQHFQEKVESLEQEA 371
      : : || | || : : : | : : : | | : | | : | : |
Db      414 SQKRLEESHREKVTRVMKDWSDL EKYQDMRLADPKAAQSFQKQRTARFQTSVQALEEEG 473
Qy      372 ANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLKKYVRAEQKDRQ 431
      | : | | | | | : | : | : | | | | | | : | : | |
Db      474 NAEKHQLAAMHQQRVLAHINQRKREAMTCYTQALTEQPPNAHHVEKCLQKLLRALHKDRA 533
Qy      432 HTLKHFEH-VRMVDP---KKAQIIRSQVMTHLRVIYERMNQSLSLLYNVPAVAEEI---- 483
      | | | : | : | : | | : : | | : || : : | | : : |
Db      534 HALAHYRHLNLSGGPGGLEAAASERPRTLRLIDIDRAVNQSMTMLKRYPELSAKIAQLM 593
Qy      484 -----QDEV----- 487
      : : :
Db      594 NDYILALRSKDDIPGSSSLGMSEAEAGILDKYRVEIERKVAEKERLRLAEKQKQRAAE 653
Qy      488 -----DELLQKEQNYSDDLANMISE-----PRISYGNDAIM 519
      : | | : | | : | : : | | | | :
Db      654 REKLREEKLRL EAKKVDDMLKSQVAEQQSQPTQSSTQSQAQQQQQEKSLPGKELGPDAAAL 713
Qy      520 -----PSLTETKTTVELLPVNGEFSLLDLPWHSFGADSV PANTENEVEPV DARPAADRG 574
      | : | || : | | | : : | : | | | |
Db      714 VTAANPNLETTKS-----EKDLSDE---YGEATVSTTKVQTVLPTVDDDAVQRA 760
Qy      575 LTTRPGSGLTNIKTEEISEVNLD AEF RHDSGYEVHHQKLVF-----FAEDVGSNK---GA 626
      : : : : : | : : : | : | : |
Db      761 VEDVAAA-----VAHQEAEPQVQHFMTHDLGHRESSFSRLRREFAQHAHA AKEGRNV 811
Qy      627 IIGLMVGGVVIATVIVITLVMLKKKQYTSIH-HGVVEVDAAVTP-----EERHLSKMQQ 679
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Db      812 YFTLSFAGIALMAAVFVGVA VAKWRTSRSPHAQGFIEVDQNVTTTHPIVREEKIVPNMQI 871
Qy      680 NGYENPTYKFFE 691
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Db      872 NGYENPTYKYFE 883

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RESULT 14

S38344

CDEI-binding protein - mouse (fragment)

C;Species: Mus musculus (house mouse)

C;Date: 19-May-1994 #sequence\_revision 26-May-1995 #text\_change 03-May-1996

C;Accession: S38344  
 R;Hanes, J.; von der Kammer, H.; Kristjansson, G.I.; Scheit, K.H.  
 Biochim. Biophys. Acta 1216, 154-156, 1993  
 A;Title: The complete cDNA coding sequence for the mouse CDEI binding protein.  
 A;Reference number: S38344; MUID:94032480; PMID:8218408  
 A;Accession: S38344  
 A;Status: preliminary  
 A;Molecule type: mRNA  
 A;Residues: 1-246 <HAN>  
 A;Cross-references: EMBL:Z22592  
 C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type  
 proteinase inhibitor homology

Query Match 19.3%; Score 706; DB 2; Length 246;  
 Best Local Similarity 51.5%; Pred. No. 2.4e-30;  
 Matches 136; Conservative 35; Mismatches 51; Indels 42; Gaps 7;

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Qy      5 LALLLLAAWTARALEV-----PTDGNAG---LLAEPQIAMFCGRLNMHMNVQNGKWSDSP 56
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Db      15 LLVLLLLGLTAPAAALAGYIEALAANAGTGFAVAEPQIAMLCGKLNMHVNIQTGWEPDP 74

Qy      57 SGTKTCTIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYR 116
      :|||:|: ||| :||| ||:|||||:||||| ||| |||:| :|||: | |||:
Db      75 TGTKSCLGTKEEVLQYCQEIYPELQITNVMEANQPVNIDSWCRRDKRQCKS--HIVIPFK 132

Qy     117 CLVGEFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGI 176
      ||||| ||| ||| :| |||: ||| | |||: || | : | : |||||:
Db     133 CLVGEFVSDVLLVPDNCQFFHQERMEVCEKHQRWHTLVKEACLTEGLTLYSYGMLLPCGV 192

Qy     177 DKFRGVEFVCCPLAEESDNVDSADAEEDSDVWGGADTDYADGSEDKVVEVAEEEEVAE 236
      |:| | |:|||  :: |||  | : |||
Db     193 DQFHGTEYVCCP---QTKTVDS-----DSTMSKEEEEE--- 222

Qy     237 VEEEEADDED-DEDGDEVEEEAE 259
      ||:| |:|| | | | ||:
Db     223 -EEDEEEDDYDLDKSEFPTEAD 245

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# RESULT 15

PQ0438

Alzheimer's disease amyloid A4 protein precursor - rabbit (fragment)

C;Species: Oryctolagus cuniculus (domestic rabbit)

C;Date: 30-Sep-1993 #sequence\_revision 19-Oct-1995 #text\_change 19-Oct-1995

C;Accession: PQ0438; C60045

R;Davidson, J.S.; West, R.L.; Kotikalapudi, P.; Maroun, L.E.

Biochem. Biophys. Res. Commun. 188, 905-911, 1992

A;Title: Sequence and methylation in the beta/A4 region of the rabbit amyloid precursor protein gene.

A;Reference number: PQ0438; MUID:93075180; PMID:1445331

A;Accession: PQ0438

A;Molecule type: DNA

A;Residues: 1-82 <DAV>

A;Cross-references: GB:M83558; GB:M83657

R;Johnstone, E.M.; Chaney, M.O.; Norris, F.H.; Pascual, R.; Little, S.P.

Brain Res. Mol. Brain Res. 10, 299-305, 1991



A;Title: Conservation of the sequence of the Alzheimer's disease amyloid peptide in dog, polar bear and five other mammals by cross-species polymerase chain reaction analysis.

A;Reference number: A60045; MUID:92017079; PMID:1656157

A;Accession: C60045

A;Molecule type: mRNA

A;Residues: 12-68 <JOH>

A;Cross-references: EMBL:X56129

C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology

C;Keywords: alternative splicing; Alzheimer's disease; amyloid; Down's syndrome

Query Match 11.0%; Score 403; DB 2; Length 82;  
Best Local Similarity 97.6%; Pred. No. 5e-15;  
Matches 80; Conservative 1; Mismatches 1; Indels 0; Gaps 0;

Qy 581 SGLTNIKTEEISEVNLDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATV 640  
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Db 1 SGLTNIKTEEISEVKMDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATV 60

Qy 641 IVITLVMLKKKQYTSIHGGVVE 662  
|||||||  
Db 61 IVITLVMLKKKQYTSIHGGVVE 82

Search completed: July 26, 2004, 12:47:27

Job time : 15.6667 secs

OM protein - protein search, using sw model

Run on: July 26, 2004, 12:46:43 ; Search time 44.3333 Seconds  
(without alignments)  
4923.349 Million cell updates/sec

Title: US-09-806-194A-18  
Perfect score: 3651  
Sequence: 1 MLPGLALLLLAAWTARALEV.....QQNGYENPTYKFFEQMQNKK 697

Scoring table: BLOSUM62  
Gapop 10.0 , Gapext 0.5

Searched: 1288442 seqs, 313154207 residues

Total number of hits satisfying chosen parameters: 1288442

Minimum DB seq length: 0  
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%  
Maximum Match 100%  
Listing first 45 summaries

Database : Published Applications\_AA:\*

- 1: /cgn2\_6/ptodata/1/pubpaa/US07\_PUBCOMB.pep:\*
- 2: /cgn2\_6/ptodata/1/pubpaa/PCT\_NEW\_PUB.pep:\*
- 3: /cgn2\_6/ptodata/1/pubpaa/US06\_NEW\_PUB.pep:\*
- 4: /cgn2\_6/ptodata/1/pubpaa/US06\_PUBCOMB.pep:\*
- 5: /cgn2\_6/ptodata/1/pubpaa/US07\_NEW\_PUB.pep:\*
- 6: /cgn2\_6/ptodata/1/pubpaa/PCTUS\_PUBCOMB.pep:\*
- 7: /cgn2\_6/ptodata/1/pubpaa/US08\_NEW\_PUB.pep:\*
- 8: /cgn2\_6/ptodata/1/pubpaa/US08\_PUBCOMB.pep:\*
- 9: /cgn2\_6/ptodata/1/pubpaa/US09A\_PUBCOMB.pep:\*
- 10: /cgn2\_6/ptodata/1/pubpaa/US09B\_PUBCOMB.pep:\*
- 11: /cgn2\_6/ptodata/1/pubpaa/US09C\_PUBCOMB.pep:\*
- 12: /cgn2\_6/ptodata/1/pubpaa/US09\_NEW\_PUB.pep:\*
- 13: /cgn2\_6/ptodata/1/pubpaa/US10A\_PUBCOMB.pep:\*
- 14: /cgn2\_6/ptodata/1/pubpaa/US10B\_PUBCOMB.pep:\*
- 15: /cgn2\_6/ptodata/1/pubpaa/US10C\_PUBCOMB.pep:\*
- 16: /cgn2\_6/ptodata/1/pubpaa/US10\_NEW\_PUB.pep:\*
- 17: /cgn2\_6/ptodata/1/pubpaa/US60\_NEW\_PUB.pep:\*
- 18: /cgn2\_6/ptodata/1/pubpaa/US60\_PUBCOMB.pep:\*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

#### SUMMARIES

Result	Query					
No.	Score	Match	Length	DB	ID	Description

1	3651	100.0	697	9	US-09-794-927-18	Sequence 18, Appl
2	3651	100.0	697	9	US-09-795-847-18	Sequence 18, Appl
3	3651	100.0	697	9	US-09-794-743-18	Sequence 18, Appl
4	3651	100.0	697	9	US-09-794-748-18	Sequence 18, Appl
5	3651	100.0	697	9	US-09-794-925-18	Sequence 18, Appl
6	3651	100.0	697	9	US-09-681-442-18	Sequence 18, Appl
7	3651	100.0	697	10	US-09-869-414-18	Sequence 18, Appl
8	3651	100.0	697	10	US-09-548-366-18	Sequence 18, Appl
9	3651	100.0	697	12	US-10-652-927-18	Sequence 18, Appl
10	3651	100.0	697	12	US-10-652-830-18	Sequence 18, Appl
11	3643	99.8	697	9	US-09-794-927-16	Sequence 16, Appl
12	3643	99.8	697	9	US-09-795-847-16	Sequence 16, Appl
13	3643	99.8	697	9	US-09-794-743-16	Sequence 16, Appl
14	3643	99.8	697	9	US-09-794-748-16	Sequence 16, Appl
15	3643	99.8	697	9	US-09-794-925-16	Sequence 16, Appl
16	3643	99.8	697	9	US-09-681-442-16	Sequence 16, Appl
17	3643	99.8	697	10	US-09-869-414-16	Sequence 16, Appl
18	3643	99.8	697	10	US-09-548-366-16	Sequence 16, Appl
19	3643	99.8	697	12	US-10-652-927-16	Sequence 16, Appl
20	3643	99.8	697	12	US-10-652-830-16	Sequence 16, Appl
21	3641	99.7	695	9	US-09-794-927-12	Sequence 12, Appl
22	3641	99.7	695	9	US-09-795-847-12	Sequence 12, Appl
23	3641	99.7	695	9	US-09-794-743-12	Sequence 12, Appl
24	3641	99.7	695	9	US-09-794-748-12	Sequence 12, Appl
25	3641	99.7	695	9	US-09-794-925-12	Sequence 12, Appl
26	3641	99.7	695	9	US-09-681-442-12	Sequence 12, Appl
27	3641	99.7	695	10	US-09-869-414-12	Sequence 12, Appl
28	3641	99.7	695	10	US-09-548-366-12	Sequence 12, Appl
29	3641	99.7	695	12	US-10-652-927-12	Sequence 12, Appl
30	3641	99.7	695	12	US-10-652-830-12	Sequence 12, Appl
31	3641	99.7	695	15	US-10-427-208-46	Sequence 46, Appl
32	3638	99.6	697	9	US-09-794-927-20	Sequence 20, Appl
33	3638	99.6	697	9	US-09-795-847-20	Sequence 20, Appl
34	3638	99.6	697	9	US-09-794-743-20	Sequence 20, Appl
35	3638	99.6	697	9	US-09-794-748-20	Sequence 20, Appl
36	3638	99.6	697	9	US-09-794-925-20	Sequence 20, Appl
37	3638	99.6	697	9	US-09-681-442-20	Sequence 20, Appl
38	3638	99.6	697	10	US-09-869-414-20	Sequence 20, Appl
39	3638	99.6	697	10	US-09-548-366-20	Sequence 20, Appl
40	3638	99.6	697	12	US-10-652-927-20	Sequence 20, Appl
41	3638	99.6	697	12	US-10-652-830-20	Sequence 20, Appl
42	3637	99.6	695	15	US-10-427-208-25	Sequence 25, Appl
43	3637	99.6	695	15	US-10-427-208-27	Sequence 27, Appl
44	3637	99.6	695	15	US-10-427-208-28	Sequence 28, Appl
45	3636	99.6	695	15	US-10-427-208-31	Sequence 31, Appl

#### ALIGNMENTS

##### RESULT 1

US-09-794-927-18

; Sequence 18, Application US/09794927

; Patent No. US20010016324A1

; GENERAL INFORMATION:

; APPLICANT: Gurney, Mark E.

```

; APPLICANT: Bienkowski, Michael J.
; APPLICANT: Heinrikson, Robert L.
; APPLICANT: Parodi, Luis A.
; APPLICANT: Yan, Riqiang
; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,
AND
; TITLE OF INVENTION: USES
; TITLE OF INVENTION: THEREFOR
; FILE REFERENCE: 28341/6280FG
; CURRENT APPLICATION NUMBER: US/09/794,927
; CURRENT FILING DATE: 2001-02-27
; PRIOR APPLICATION NUMBER: 09/416,901
; PRIOR FILING DATE: 1999-10-13
; PRIOR APPLICATION NUMBER: 60/155,493
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 09/404,133
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 73
; SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 18
; LENGTH: 697
; TYPE: PRT
; ORGANISM: Homo sapiens
US-09-794-927-18

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Query Match          100.0%; Score 3651; DB 9; Length 697;
Best Local Similarity 100.0%; Pred. No. 1.1e-223;
Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
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Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG 120
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Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
        |
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
        |
Db    181 GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTTSIATTTTTTTTSESVEEVVRVPTTAASTPDAV 300
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Db    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTTSIATTTTTTTTSESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360
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RESULT 2

US-09-795-847-18

; Sequence 18, Application US/09795847

; Patent No. US20010018208A1

; GENERAL INFORMATION:

; APPLICANT: Gurney, Mark E.

; APPLICANT: Bienkowski, Michael J.

; APPLICANT: Heinrikson, Robert L.

; APPLICANT: Parodi, Luis A.

; APPLICANT: Yan, Riqiang

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,  
AND

; TITLE OF INVENTION: USES

; TITLE OF INVENTION: THEREFOR

; FILE REFERENCE: 28341/6280DE

; CURRENT APPLICATION NUMBER: US/09/795,847

; CURRENT FILING DATE: 2001-02-28

; PRIOR APPLICATION NUMBER: 09/416,901

; PRIOR FILING DATE: 1999-10-13

; PRIOR APPLICATION NUMBER: 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 73

; SOFTWARE: PatentIn Ver. 2.0

; SEQ ID NO 18

; LENGTH: 697

; TYPE: PRT

; ORGANISM: Homo sapiens  
US-09-795-847-18

Query Match 100.0%; Score 3651; DB 9; Length 697;  
Best Local Similarity 100.0%; Pred. No. 1.1e-223;  
Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy    181 GVEFVCCPLAEESDNVDSADAEEDDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
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Db    181 GVEFVCCPLAEESDNVDSADAEEDDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

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        ||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL 540

Qy    541 DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600
        ||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    541 DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600

Qy    601 RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITL VMLKKKQYTSIHHGV 660
        ||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    601 RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITL VMLKKKQYTSIHHGV 660

Qy    661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK 697
        ||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK 697
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RESULT 3

US-09-794-743-18  
; Sequence 18, Application US/09794743  
; Patent No. US20010021391A1  
; GENERAL INFORMATION:  
; APPLICANT: Gurney, Mark E.  
; APPLICANT: Bienkowski, Michael J.  
; APPLICANT: Heinrikson, Robert L.  
; APPLICANT: Parodi, Luis A.  
; APPLICANT: Yan, Riqiang  
; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,  
AND  
; TITLE OF INVENTION: USES  
; TITLE OF INVENTION: THEREFOR  
; FILE REFERENCE: 28341/6280BC  
; CURRENT APPLICATION NUMBER: US/09/794,743  
; CURRENT FILING DATE: 2001-02-27  
; PRIOR APPLICATION NUMBER: 09/416,901  
; PRIOR FILING DATE: 1999-10-13  
; PRIOR APPLICATION NUMBER: 60/155,493  
; PRIOR FILING DATE: 1999-09-23  
; PRIOR APPLICATION NUMBER: 09/404,133  
; PRIOR FILING DATE: 1999-09-23  
; PRIOR APPLICATION NUMBER: PCT/US99/20881  
; PRIOR FILING DATE: 1999-09-23  
; PRIOR APPLICATION NUMBER: 60/101,594  
; PRIOR FILING DATE: 1998-09-24  
; NUMBER OF SEQ ID NOS: 73  
; SOFTWARE: PatentIn Ver. 2.0  
; SEQ ID NO 18  
; LENGTH: 697  
; TYPE: PRT  
; ORGANISM: Homo sapiens  
US-09-794-743-18

Query Match 100.0%; Score 3651; DB 9; Length 697;  
Best Local Similarity 100.0%; Pred. No. 1.1e-223;  
Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE	240
Qy	241	EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300

Qy 301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360  
 |||  
 Db 301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360

Qy 361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420  
 |||  
 Db 361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480  
 |||  
 Db 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480

Qy 481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540  
 |||  
 Db 481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540

Qy 541 DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600  
 |||  
 Db 541 DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600

Qy 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660  
 |||  
 Db 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660

Qy 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK 697  
 |||  
 Db 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK 697

RESULT 4

US-09-794-748-18

; Sequence 18, Application US/09794748

; Patent No. US20020037315A1

; GENERAL INFORMATION:

; APPLICANT: Gurney, Mark E.

; APPLICANT: Bienkowski, Michael J.

; APPLICANT: Heinrikson, Robert L.

; APPLICANT: Parodi, Luis A.

; APPLICANT: Yan, Riqiang

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,  
 AND

; TITLE OF INVENTION: USES

; TITLE OF INVENTION: THEREFOR

; FILE REFERENCE: 28341/6280JL

; CURRENT APPLICATION NUMBER: US/09/794,748

; CURRENT FILING DATE: 2001-02-27

; PRIOR APPLICATION NUMBER: 09/416,901

; PRIOR FILING DATE: 1999-10-13

; PRIOR APPLICATION NUMBER: 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 60/101,594

; PRIOR FILING DATE: 1998-09-24



; NUMBER OF SEQ ID NOS: 73  
; SOFTWARE: PatentIn Ver. 2.0  
; SEQ ID NO 18  
; LENGTH: 697  
; TYPE: PRT  
; ORGANISM: Homo sapiens  
US-09-794-748-18

Query Match 100.0%; Score 3651; DB 9; Length 697;  
Best Local Similarity 100.0%; Pred. No. 1.1e-223;  
Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
        |||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG 120
        |||
Db     61 TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
        |||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
        |||
Db    181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
        |||
Db    241 EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360
        |||
Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360

Qy    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
        |||
Db    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480
        |||
Db    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480

Qy    481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL 540
        |||
Db    481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL 540

Qy    541 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600
        |||
Db    541 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600

Qy    601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVM LKKKQYTSIHHGV 660
        |||
Db    601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVM LKKKQYTSIHHGV 660

Qy    661 VEVDAAVTPEERHLSKMQONGYENPTYKFFEQMQNKK 697
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Db 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK 697

RESULT 5

US-09-794-925-18

; Sequence 18, Application US/09794925

; Patent No. US20020064819A1

; GENERAL INFORMATION:

; APPLICANT: Gurney, Mark E.

; APPLICANT: Bienkowski, Michael J.

; APPLICANT: Heinrikson, Robert L.

; APPLICANT: Parodi, Luis A.

; APPLICANT: Yan, Riqiang

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR, AND USES

; TITLE OF INVENTION: THEREFOR

; FILE REFERENCE: 28341/6280HI

; CURRENT APPLICATION NUMBER: US/09/794,925

; CURRENT FILING DATE: 2001-02-27

; PRIOR APPLICATION NUMBER: 09/416,901

; PRIOR FILING DATE: 1999-10-13

; PRIOR APPLICATION NUMBER: 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 73

; SOFTWARE: PatentIn Ver. 2.0

; SEQ ID NO 18

; LENGTH: 697

; TYPE: PRT

; ORGANISM: Homo sapiens

US-09-794-925-18

Query Match 100.0%; Score 3651; DB 9; Length 697;

Best Local Similarity 100.0%; Pred. No. 1.1e-223;

Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGTK 60

Db 1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGTK 60

Qy 61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Db 61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy 121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Db 121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy 181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Db 181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy	241	EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTTSESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTTSESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF	600
Db	541	DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF	600
Qy	601	RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV	660
Db	601	RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK	697
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK	697

# RESULT 6

US-09-681-442-18

; Sequence 18, Application US/09681442

; Patent No. US20020081634A1

## ; GENERAL INFORMATION:

; APPLICANT: Gurney, Mark E.

; APPLICANT: Bienkowski, Michael J.

; APPLICANT: Heinrikson, Robert L.

; APPLICANT: Parodi, Luis A.

; APPLICANT: Yan, Riqiang

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR, AND USES

; TITLE OF INVENTION: THEREFOR

; FILE REFERENCE: 28341/6280FG

; CURRENT APPLICATION NUMBER: US/09/681,442

; CURRENT FILING DATE: 2001-04-05

; PRIOR APPLICATION NUMBER: 09/416,901

; PRIOR FILING DATE: 1999-10-13

; PRIOR APPLICATION NUMBER: 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23  
; PRIOR APPLICATION NUMBER: 60/101,594  
; PRIOR FILING DATE: 1998-09-24  
; NUMBER OF SEQ ID NOS: 73  
; SOFTWARE: PatentIn Ver. 2.0  
; SEQ ID NO 18  
; LENGTH: 697  
; TYPE: PRT  
; ORGANISM: Homo sapiens  
US-09-681-442-18

Query Match 100.0%; Score 3651; DB 9; Length 697;  
Best Local Similarity 100.0%; Pred. No. 1.1e-223;  
Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVI	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVI	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVP	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVP	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFS	540
Db	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFS	540
Qy	541	DDLQPWHSFGADSVANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVN	600
Db	541	DDLQPWHSFGADSVANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVN	600
Qy	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSI	660



Qy	241	EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAENERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAAENERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF	600
Db	541	DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF	600
Qy	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIH HGV	660
Db	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIH HGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697

RESULT 8

US-09-548-366-18

; Sequence 18, Application US/09548366

; Publication No. US20030104365A1

; GENERAL INFORMATION:

; APPLICANT: Gurney, Mark E.

; APPLICANT: Bienkowski, Michael J.

; APPLICANT: Heinrikson, Robert L.

; APPLICANT: Parodi, Luis A.

; APPLICANT: Yan, Riqiang

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR, AND

; TITLE OF INVENTION: USES THEREFOR

; FILE REFERENCE: 28341/6280A

; CURRENT APPLICATION NUMBER: US/09/548,366

; CURRENT FILING DATE: 2000-04-12

; PRIOR APPLICATION NUMBER: 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 65  
; SOFTWARE: PatentIn Ver. 2.0  
; SEQ ID NO 18  
; LENGTH: 697  
; TYPE: PRT  
; ORGANISM: Homo sapiens  
US-09-548-366-18

Query Match 100.0%; Score 3651; DB 10; Length 697;  
Best Local Similarity 100.0%; Pred. No. 1.1e-223;  
Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
        |||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG 120
        |||
Db     61 TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
        |||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
        |||
Db    181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
        |||
Db    241 EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360
        |||
Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360

Qy    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
        |||
Db    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480
        |||
Db    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480

Qy    481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL 540
        |||
Db    481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL 540

Qy    541 DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600
        |||
Db    541 DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600

Qy    601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVM LKKKQYTSIHHGV 660
        |||
Db    601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVM LKKKQYTSIHHGV 660

Qy    661 VEVDAAVTPEERHLSKMQONGYENPTYKFFEQM QNKK 697
```

|||||  
Db 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697

RESULT 9

US-10-652-927-18

; Sequence 18, Application US/10652927

; Publication No. US20040043408A1

; GENERAL INFORMATION:

; APPLICANT: Gurney et al.

; TITLE OF INVENTION: Alzheimer's Disease Secretase, APP Substrates Therefor  
and Uses

; TITLE OF INVENTION: Therefor

; FILE REFERENCE: 29915/6280N3

; CURRENT APPLICATION NUMBER: US/10/652,927

; CURRENT FILING DATE: 2003-08-29

; PRIOR APPLICATION NUMBER: 09/794,925

; PRIOR FILING DATE: 2001-02-27

; PRIOR APPLICATION NUMBER: 09/416,901

; PRIOR FILING DATE: 1999-10-13

; PRIOR APPLICATION NUMBER: 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 74

; SOFTWARE: PatentIn Ver. 2.0

; SEQ ID NO 18

; LENGTH: 697

; TYPE: PRT

; ORGANISM: Homo sapiens

US-10-652-927-18

Query Match 100.0%; Score 3651; DB 12; Length 697;

Best Local Similarity 100.0%; Pred. No. 1.1e-223;

Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60  
|  
Db 1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy 61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVI PYRCLVG 120  
|  
Db 61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVI PYRCLVG 120

Qy 121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180  
|  
Db 121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy 181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE 240  
|  
Db 181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE 240

Qy 241 EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300



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Db      241  EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
Qy      301  DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360
Db      301  DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360
Qy      361  QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
Db      361  QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
Qy      421  KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480
Db      421  KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480
Qy      481  EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540
Db      481  EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540
Qy      541  DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600
Db      541  DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600
Qy      601  RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660
Db      601  RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660
Qy      661  VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK 697
Db      661  VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK 697

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RESULT 10

US-10-652-830-18

; Sequence 18, Application US/10652830

; Publication No. US20040048303A1

; GENERAL INFORMATION:

; APPLICANT: Gurney et al.

; TITLE OF INVENTION: Alzheimer's Disease Secretase, APP Substrates Therefor and Uses

; TITLE OF INVENTION: Therefor

; FILE REFERENCE: 29915/6280N1

; CURRENT APPLICATION NUMBER: US/10/652,830

; CURRENT FILING DATE: 2003-08-29

; PRIOR APPLICATION NUMBER: 09/794,925

; PRIOR FILING DATE: 2001-02-27

; PRIOR APPLICATION NUMBER: 09/416,901

; PRIOR FILING DATE: 1999-10-13

; PRIOR APPLICATION NUMBER: 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 74

; SOFTWARE: PatentIn Ver. 2.0  
; SEQ ID NO 18  
; LENGTH: 697  
; TYPE: PRT  
; ORGANISM: Homo sapiens  
US-10-652-830-18

Query Match 100.0%; Score 3651; DB 12; Length 697;  
Best Local Similarity 100.0%; Pred. No. 1.1e-223;  
Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
      |||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVPIPYRCLVG 120
      |||
Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVPIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
      |||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
      |||
Db    181 GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
      |||
Db    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360
      |||
Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360

Qy    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
      |||
Db    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480
      |||
Db    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480

Qy    481 EEIQDEVDELLQKEQNYSDVLANMISEPRI SYGNDALMPSLTETKTTVELLPVNGEFSL 540
      |||
Db    481 EEIQDEVDELLQKEQNYSDVLANMISEPRI SYGNDALMPSLTETKTTVELLPVNGEFSL 540

Qy    541 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600
      |||
Db    541 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600

Qy    601 RHDSGYEVHHQKL VFFAEDVGSNKGAI IGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660
      |||
Db    601 RHDSGYEVHHQKL VFFAEDVGSNKGAI IGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660

Qy    661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK 697
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## RESULT 11

US-09-794-927-16

; Sequence 16, Application US/09794927

; Patent No. US20010016324A1

; GENERAL INFORMATION:

; APPLICANT: Gurney, Mark E.

; APPLICANT: Bienkowski, Michael J.

; APPLICANT: Heinrikson, Robert L.

; APPLICANT: Parodi, Luis A.

; APPLICANT: Yan, Riqiang

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,  
AND

; TITLE OF INVENTION: USES

; TITLE OF INVENTION: THEREFOR

; FILE REFERENCE: 28341/6280FG

; CURRENT APPLICATION NUMBER: US/09/794,927

; CURRENT FILING DATE: 2001-02-27

; PRIOR APPLICATION NUMBER: 09/416,901

; PRIOR FILING DATE: 1999-10-13

; PRIOR APPLICATION NUMBER: 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 73

; SOFTWARE: PatentIn Ver. 2.0

; SEQ ID NO 16

; LENGTH: 697

; TYPE: PRT

; ORGANISM: Homo sapiens

US-09-794-927-16

Query Match 99.8%; Score 3643; DB 9; Length 697;

Best Local Similarity 99.7%; Pred. No. 3.4e-223;

Matches 695; Conservative 1; Mismatches 1; Indels 0; Gaps 0;

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Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
        |||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
        |||
Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
        |||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE 240
        |||
Db    181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE 240
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Qy 241 EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300  
 |||  
 Db 241 EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy 301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360  
 |||  
 Db 301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360

Qy 361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420  
 |||  
 Db 361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480  
 |||  
 Db 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480

Qy 481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540  
 |||  
 Db 481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540

Qy 541 DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600  
 ||| :|||  
 Db 541 DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMD AEF 600

Qy 601 RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660  
 |||  
 Db 601 RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660

Qy 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK 697  
 |||  
 Db 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK 697

RESULT 12

US-09-795-847-16

; Sequence 16, Application US/09795847

; Patent No. US20010018208A1

; GENERAL INFORMATION:

; APPLICANT: Gurney, Mark E.

; APPLICANT: Bienkowski, Michael J.

; APPLICANT: Heinrikson, Robert L.

; APPLICANT: Parodi, Luis A.

; APPLICANT: Yan, Riqiang

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,  
 AND

; TITLE OF INVENTION: USES

; TITLE OF INVENTION: THEREFOR

; FILE REFERENCE: 28341/6280DE

; CURRENT APPLICATION NUMBER: US/09/795,847

; CURRENT FILING DATE: 2001-02-28

; PRIOR APPLICATION NUMBER: 09/416,901

; PRIOR FILING DATE: 1999-10-13

; PRIOR APPLICATION NUMBER: 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881  
; PRIOR FILING DATE: 1999-09-23  
; PRIOR APPLICATION NUMBER: 60/101,594  
; PRIOR FILING DATE: 1998-09-24  
; NUMBER OF SEQ ID NOS: 73  
; SOFTWARE: PatentIn Ver. 2.0  
; SEQ ID NO 16  
; LENGTH: 697  
; TYPE: PRT  
; ORGANISM: Homo sapiens  
US-09-795-847-16

Query Match 99.8%; Score 3643; DB 9; Length 697;  
Best Local Similarity 99.7%; Pred. No. 3.4e-223;  
Matches 695; Conservative 1; Mismatches 1; Indels 0; Gaps 0;

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Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHNMNVQNGKWDSDPSGTK 60
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHNMNVQNGKWDSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVI PYRCLVG 120
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVI PYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV 300
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360

Qy    361 QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    361 QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480

Qy    481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTLTETKTTVELLPVNGEFSL 540
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTLTETKTTVELLPVNGEFSL 540

Qy    541 DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEI SEVNLD AEF 600
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    541 DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEI SEVKMD AEF 600

Qy    601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660
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Db          601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV 660
Qy          661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK 697
Db          661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK 697

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RESULT 13

US-09-794-743-16

; Sequence 16, Application US/09794743

; Patent No. US20010021391A1

; GENERAL INFORMATION:

; APPLICANT: Gurney, Mark E.

; APPLICANT: Bienkowski, Michael J.

; APPLICANT: Heinrikson, Robert L.

; APPLICANT: Parodi, Luis A.

; APPLICANT: Yan, Riqiang

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,  
AND

; TITLE OF INVENTION: USES

; TITLE OF INVENTION: THEREFOR

; FILE REFERENCE: 28341/6280BC

; CURRENT APPLICATION NUMBER: US/09/794,743

; CURRENT FILING DATE: 2001-02-27

; PRIOR APPLICATION NUMBER: 09/416,901

; PRIOR FILING DATE: 1999-10-13

; PRIOR APPLICATION NUMBER: 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 73

; SOFTWARE: PatentIn Ver. 2.0

; SEQ ID NO 16

; LENGTH: 697

; TYPE: PRT

; ORGANISM: Homo sapiens

US-09-794-743-16

Query Match 99.8%; Score 3643; DB 9; Length 697;

Best Local Similarity 99.7%; Pred. No. 3.4e-223;

Matches 695; Conservative 1; Mismatches 1; Indels 0; Gaps 0;

```

Qy          1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
Db          1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
Qy          61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIRCLVG 120
Db          61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIRCLVG 120
Qy          121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

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Db 121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy 181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE 240  
 |||

Db 181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE 240

Qy 241 EADDDDEDDEDGDEVEEEAEEPYYEATERTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV 300  
 |||

Db 241 EADDDDEDDEDGDEVEEEAEEPYYEATERTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy 301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360  
 |||

Db 301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360

Qy 361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420  
 |||

Db 361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480  
 |||

Db 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480

Qy 481 EEIQDEVDELLOKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540  
 |||

Db 481 EEIQDEVDELLOKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540

Qy 541 DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600  
 ||| :|||

Db 541 DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMD AEF 600

Qy 601 RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVM LKKKQYTSIHHGV 660  
 |||

Db 601 RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVM LKKKQYTSIHHGV 660

Qy 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK 697  
 |||

Db 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK 697

RESULT 14

US-09-794-748-16

; Sequence 16, Application US/09794748

; Patent No. US20020037315A1

; GENERAL INFORMATION:

; APPLICANT: Gurney, Mark E.

; APPLICANT: Bienkowski, Michael J.

; APPLICANT: Heinrikson, Robert L.

; APPLICANT: Parodi, Luis A.

; APPLICANT: Yan, Riqiang

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR, AND

; TITLE OF INVENTION: USES

; TITLE OF INVENTION: THEREFOR

; FILE REFERENCE: 28341/6280JL

; CURRENT APPLICATION NUMBER: US/09/794,748

; CURRENT FILING DATE: 2001-02-27

; PRIOR APPLICATION NUMBER: 09/416,901

; PRIOR FILING DATE: 1999-10-13  
; PRIOR APPLICATION NUMBER: 60/155,493  
; PRIOR FILING DATE: 1999-09-23  
; PRIOR APPLICATION NUMBER: 09/404,133  
; PRIOR FILING DATE: 1999-09-23  
; PRIOR APPLICATION NUMBER: PCT/US99/20881  
; PRIOR FILING DATE: 1999-09-23  
; PRIOR APPLICATION NUMBER: 60/101,594  
; PRIOR FILING DATE: 1998-09-24  
; NUMBER OF SEQ ID NOS: 73  
; SOFTWARE: PatentIn Ver. 2.0  
; SEQ ID NO 16  
; LENGTH: 697  
; TYPE: PRT  
; ORGANISM: Homo sapiens  
US-09-794-748-16

Query Match 99.8%; Score 3643; DB 9; Length 697;  
Best Local Similarity 99.7%; Pred. No. 3.4e-223;  
Matches 695; Conservative 1; Mismatches 1; Indels 0; Gaps 0;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEEEE	240
Qy	241	EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL	540



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Qy      541 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600
          |||
Db      541 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMD AEF 600

Qy      601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660
          |||
Db      601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660

Qy      661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK 697
          |||
Db      661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK 697

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RESULT 15

US-09-794-925-16

; Sequence 16, Application US/09794925

; Patent No. US20020064819A1

; GENERAL INFORMATION:

; APPLICANT: Gurney, Mark E.

; APPLICANT: Bienkowski, Michael J.

; APPLICANT: Heinrikson, Robert L.

; APPLICANT: Parodi, Luis A.

; APPLICANT: Yan, Riqiang

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR, AND USES

; TITLE OF INVENTION: THEREFOR

; FILE REFERENCE: 28341/6280HI

; CURRENT APPLICATION NUMBER: US/09/794,925

; CURRENT FILING DATE: 2001-02-27

; PRIOR APPLICATION NUMBER: 09/416,901

; PRIOR FILING DATE: 1999-10-13

; PRIOR APPLICATION NUMBER: 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 73

; SOFTWARE: PatentIn Ver. 2.0

; SEQ ID NO 16

; LENGTH: 697

; TYPE: PRT

; ORGANISM: Homo sapiens

US-09-794-925-16

Query Match 99.8%; Score 3643; DB 9; Length 697;

Best Local Similarity 99.7%; Pred. No. 3.4e-223;

Matches 695; Conservative 1; Mismatches 1; Indels 0; Gaps 0;

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Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGTK 60
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Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGTK 60

Qy      61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
          |||

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Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLANMISEPRISYGN DALMP SLTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLANMISEPRISYGN DALMP SLTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVN L DAEF	600
		:	
Db	541	DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEV KMDAEF	600
Qy	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV	660
Db	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK	697
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK	697

Search completed: July 26, 2004, 13:00:43  
Job time : 45.3333 secs



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2	3379	92.5	751	13	Q9DGJ7	Q9dgj7 gallus gall
3	3206	87.8	693	13	Q98SG0	Q98sg0 xenopus lae
4	3182	87.2	695	13	Q98SF9	Q98sf9 xenopus lae
5	3180	87.1	695	13	Q7ZXQ0	Q7zxq0 xenopus lae
6	3095	84.8	747	13	Q91963	Q91963 xenopus. ap
7	2956.5	81.0	699	13	Q57394	Q57394 narke japon
8	2759.5	75.6	569	13	Q9PVL1	Q9pvl1 gallus gall
9	2605	71.4	534	13	Q93296	Q93296 gallus gall
10	2562	70.2	678	13	Q7ZZT1	Q7zzt1 brachydanio
11	2524	69.1	738	13	Q90W28	Q90w28 brachydanio
12	2487.5	68.1	694	13	Q8UUR9	Q8uur9 brachydanio
13	2334	63.9	612	13	Q9I9E7	Q9i9e7 brachydanio
14	1920	52.6	384	11	Q8BPC7	Q8bpc7 mus musculu
15	1762	48.3	695	4	Q13861	Q13861 homo sapien
16	1746.5	47.8	669	4	Q14662	Q14662 homo sapien
17	1737	47.6	707	11	Q80US7	Q80us7 mus musculu
18	1735	47.5	695	11	Q64348	Q64348 mus musculu
19	1726	47.3	715	11	Q7TT34	Q7tt34 mus musculu
20	1701	46.6	763	11	Q61482	Q61482 mus musculu
21	1699	46.5	751	11	Q60709	Q60709 mus musculu
22	1650	45.2	472	13	Q8UUS0	Q8uus0 brachydanio
23	1345.5	36.9	357	13	Q8UUI8	Q8uui8 brachydanio
24	1301.5	35.6	522	4	Q9BT36	Q9bt36 homo sapien
25	1082	29.6	218	11	Q8BPV5	Q8bpv5 mus musculu
26	1048.5	28.7	523	4	Q14594	Q14594 homo sapien
27	794	21.7	357	13	Q7ZZT2	Q7zzt2 brachydanio
28	771	21.1	239	13	Q8UUI7	Q8uui7 brachydanio
29	569	15.6	113	13	Q8JH58	Q8jh58 chelydra se
30	561	15.4	182	11	Q9CYS4	Q9cys4 mus musculu
31	478	13.1	97	6	Q28673	Q28673 oryctolagus
32	435.5	11.9	140	13	Q800X9	Q800x9 chelydra se
33	385.5	10.6	82	4	Q16019	Q16019 homo sapien
34	381.5	10.4	82	4	Q16014	Q16014 homo sapien
35	379.5	10.4	82	4	Q16020	Q16020 homo sapien
36	368	10.1	79	11	Q35463	Q35463 cricetulus
37	358.5	9.8	160	11	Q9QZ78	Q9qz78 cavia sp. p
38	328	9.0	208	11	Q8R0R7	Q8r0r7 mus musculu
39	239	6.5	49	6	Q97917	Q97917 bos taurus
40	196.5	5.4	727	5	Q95TG7	Q95tg7 drosophila
41	196.5	5.4	5303	5	Q9V628	Q9v628 drosophila
42	194	5.3	785	5	Q9GQ82	Q9gq82 drosophila
43	192.5	5.3	556	5	Q95S93	Q95s93 drosophila
44	192.5	5.3	1110	13	Q91255	Q91255 petromyzon
45	191.5	5.2	556	5	Q9V7I9	Q9v7i9 drosophila

# ALIGNMENTS

## RESULT 1

Q9DGJ8

ID Q9DGJ8 PRELIMINARY; PRT; 695 AA.  
AC Q9DGJ8;  
DT 01-MAR-2001 (TrEMBLrel. 16, Created)  
DT 01-MAR-2001 (TrEMBLrel. 16, Last sequence update)  
DT 01-JUN-2003 (TrEMBLrel. 24, Last annotation update)

DE Beta-amyloid precursor protein 695 isoform.  
OS Gallus gallus (Chicken).  
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
OC Archosauria; Aves; Neognathae; Galliformes; Phasianidae; Phasianinae;  
OC Gallus.  
OX NCBI\_TaxID=9031;  
RN [1]  
RP SEQUENCE FROM N.A.  
RA Sarasa M., Rodolosse A., Sorribas V.;  
RT "Cloning of full-length chicken beta-amyloid precursor protein  
RT isoforms.";  
RL Submitted (JUL-2000) to the EMBL/GenBank/DDBJ databases.  
DR EMBL; AF289218; AAG00593.1; -.  
DR HSSP; P05067; 1BA4.  
DR GO; GO:0016020; C:membrane; IEA.  
DR InterPro; IPR008155; A4\_APP.  
DR InterPro; IPR008154; A4\_extra.  
DR InterPro; IPR001255; Beta-APP.  
DR Pfam; PF02177; A4\_EXTRA; 1.  
DR Pfam; PF03494; Beta-APP; 1.  
DR PRINTS; PR00203; AMYLOIDA4.  
DR SMART; SM00006; A4\_EXTRA; 1.  
DR PROSITE; PS00319; A4\_EXTRA; 1.  
DR PROSITE; PS00320; A4\_INTRA; 1.  
SQ SEQUENCE 695 AA; 78565 MW; F201ED02AEC86D95 CRC64;

Query Match 93.7%; Score 3420; DB 13; Length 695;  
Best Local Similarity 93.7%; Pred. No. 3e-197;  
Matches 653; Conservative 18; Mismatches 22; Indels 4; Gaps 3;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGK	60
Db	1	MLPHLALLLLAAGAARALEVPADGNAGLLAEPQIAMFCGKLNMHMNVQNGKWESDPSGK	60
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGWKQCNHGHPIVVPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKLLHQERMDVCETHLHWHTVAKESCSEKSMNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDDSDVWGGADTDYADGSEDKVVE--VAEEEEVAEVE	238
Db	181	GVEFVCCPLAEESDNLDSADAEDDDSDVWGGADADYADGSDDKVVEEQPEEDEELTVVE	240
Qy	239	EEEADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPD	298
		:  :        :     :	
Db	241	DEDADDD-DDDDGDEI-EETEEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPD	298
Qy	299	AVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQ	358
Db	299	AVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQ	358
Qy	359	HFQEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNM	418
Db	359	HFQEKVESLEQEAAANERQQLVETHMARVEAMLNDRRIAENYITALQTVPPRPRHVFNM	418

Qy 419 LKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPA 478  
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 Db 419 LKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSFLYNVPA 478

Qy 479 VAEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEF 538  
 |||  
 Db 479 VAEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVDGEF 538

Qy 539 SLDDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVN LDA 598  
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 Db 539 SLDDLQPWHPFGVDSVPANTENEVEPVDARPAADRGLTTRPGSGLTNVKTEEVSEVKMDA 598

Qy 599 EFRHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITL VMLKKKQYTSIHH 658  
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 Db 599 EFRHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITL VMLKKKQYTSIHH 658

Qy 659 GVVEVDAAVTPEERHLSKMQQNGYENPTYKFFE QMQN 695  
 |||  
 Db 659 GVVEVDAAVTPEERHLSKMQQNGYENPTYKFFE QMQN 695

## RESULT 2

### Q9DGJ7

ID Q9DGJ7 PRELIMINARY; PRT; 751 AA.  
 AC Q9DGJ7;  
 DT 01-MAR-2001 (TrEMBLrel. 16, Created)  
 DT 01-MAR-2001 (TrEMBLrel. 16, Last sequence update)  
 DT 01-JUN-2003 (TrEMBLrel. 24, Last annotation update)  
 DE Beta-amyloid precursor protein 751 isoform.  
 OS Gallus gallus (Chicken).  
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
 OC Archosauria; Aves; Neognathae; Galliformes; Phasianidae; Phasianinae;  
 OC Gallus.  
 OX NCBI\_TaxID=9031;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RA Sarasa M., Rodolosse A., Sorribas V.;  
 RT "Cloning of full-length chicken beta-amyloid precursor protein  
 RT isoforms."  
 RL Submitted (JUL-2000) to the EMBL/GenBank/DDBJ databases.  
 DR EMBL; AF289219; AAG00594.1; -.  
 DR HSSP; P05067; 1BA4.  
 DR GO; GO:0016020; C:membrane; IEA.  
 DR GO; GO:0004867; F:serine protease inhibitor activity; IEA.  
 DR InterPro; IPR008155; A4\_APP.  
 DR InterPro; IPR008154; A4\_extra.  
 DR InterPro; IPR001255; Beta-APP.  
 DR InterPro; IPR002223; Kunitz\_BPTI.  
 DR Pfam; PF02177; A4\_EXTRA; 1.  
 DR Pfam; PF03494; Beta-APP; 1.  
 DR Pfam; PF00014; Kunitz\_BPTI; 1.  
 DR PRINTS; PR00203; AMYLOIDA4.  
 DR PRINTS; PR00759; BASICPTASE.  
 DR ProDom; PD000222; Kunitz\_BPTI; 1.  
 DR SMART; SM00006; A4\_EXTRA; 1.  
 DR SMART; SM00131; KU; 1.







Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVEVA--EEEEVAEVE	238
Db	180	GVEFVCCPSAAEESFSFDSADA-EDDSDAWGGADADYVDRSDDKAVEAQPDDEEEVVEVE	238
Qy	239	EEEADDDDEDDGDGEVEEEAEEPYYEATERTTSIATTTTTTTTESVEEVVRVPTTAASTPD	298
Db	239	EEETDDDED--DGDEAEEEPPEPYEATERTTSIATTTTTTTTESVEEVVRVPATAASTPD	296
Qy	299	AVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQ	358
Db	297	AVDKYLENPNDENEHDFLKAKERLEGKHKREKMSVEMKEWEEAERQAKNLPKADKKAVIQ	356
Qy	359	HFQEKVESLEQEAAANERQQLVETHMARVEAMLNDRRRLALENYITALQAVPPRPRHVFNM	418
Db	357	HFQEKVESLEQEAAANERQQLVETHMARVEAMLNDRRRIALENYITALQADPPRPRHVFNM	416
Qy	419	LKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPA	478
Db	417	LKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVINERMNQSFSLLYKVPA	476
Qy	479	VAEEIQDEVDELQKEQNYSDDLANMISEPRISYGNDAIMPSTLTETKTTVELLPVNGEF	538
Db	477	VAEEIQDEVDELQKEQNYSDDMVSNMVS DHRVSYGNDAIMPSTLSETKTTVELLPVDGEF	536
Qy	539	SLDDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLDA	598
Db	537	NIEDLQPWHSFGVDSVPANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDS	596
Qy	599	EFRHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHH	658
Db	597	EYRHDTAYEVHHQKL VFFAEVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTTIHH	656
Qy	659	GVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN	695
Db	657	GVVEVDAAVTPEERHLTKMOONGYENPTYKFFEOMON	693

DR EMBL; AJ298151; CAC37194.1; -.  
 DR HSSP; P05067; 1HZ3.  
 DR GO; GO:0016020; C:membrane; IEA.  
 DR InterPro; IPR008155; A4\_APP.  
 DR InterPro; IPR008154; A4\_extra.  
 DR InterPro; IPR001255; Beta-APP.  
 DR Pfam; PF02177; A4\_EXTRA; 1.  
 DR Pfam; PF03494; Beta-APP; 1.  
 DR PRINTS; PR00203; AMYLOIDA4.  
 DR SMART; SM00006; A4\_EXTRA; 1.  
 DR PROSITE; PS00319; A4\_EXTRA; 1.  
 DR PROSITE; PS00320; A4\_INTRA; 1.  
 KW Signal.  
 FT SIGNAL 1 18 POTENTIAL.  
 SQ SEQUENCE 695 AA; 78803 MW; DC14EB02AFB0204A CRC64;

Query Match 87.2%; Score 3182; DB 13; Length 695;  
 Best Local Similarity 87.0%; Pred. No. 6e-183;  
 Matches 607; Conservative 40; Mismatches 45; Indels 6; Gaps 5;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGK	60
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Db	1	MLPHITLLVLTA-GALALEVPADGNGGLLAEPQIAMFCGKLNMHMNVQNGKWETDVS	59
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
		:           :	
Db	60	GCIGTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKKGRKQCKSRTHIVVPYRCLVG	119
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
		:           :      :  :	
Db	120	EFVSDALLVPDKCKFLHQERMDICETHLHWHTVAKESCSEKIMSLHEYGMLLPCGIDKFR	179
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEV--AEVEEVAEVE	238
		:                           :	
Db	180	GVEFVCCPTAEESSESFDSADA-EDSDVWVGADADYVDRSDDKAVEAQPEEEEEVEVE	238
Qy	239	EEEADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVR-VPTTAASTP	297
		:	
Db	239	EEEADDD-DEDDGDETEEEPEEPEYEEATERTTSIATTTTTTTESVEEVVRVPATAVSTP	297
Qy	298	DAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAEERQAKNLPKADKKAVI	357
		:  :  :	
Db	298	DAVDKYLENPNDENEHDFLKAKEKLEKHKREKMSVMEKEWEEAEERQAKNLPKADKKAVI	357
Qy	358	QHFQEKVESLEQEAAERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFN	417
		:	
Db	358	QHFQEKVESLEQEAAERQQLVETHMARVEATLNDRRRRIALENYITALQADPPRPRHVFN	417
Qy	418	MLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVP	477
Db	418	MLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVINERMNQSFSLLYKVP	477
Qy	478	AVAEIQDEVDLLQKEQNYSDDLANMISEPRISYGNDAIMPSTETKTTVELLPVNGE	537
		:  :  :   :           :           :	
Db	478	AVAEIQDEVDLQKEQNYSDDMVSNMVSDFRVSYGNDAIMPSTETKTTVELLPVDGE	537
Qy	538	FSLDDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD	597



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Db      120 EFVSDALLVPDKCKFLHQERMDICETHLHWHTVAKESCSEKIMSLHEYGMLLPCGIDKFR 179
Qy      181 GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEV--AEEEEVAEVE 238
        |||||: ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db      180 GVEFVCCPTAEESFSDSADA-EDSDVWWGGADADYVDRSDDKAVEAQPEEEEEVVEVE 238
Qy      239 EEEADDDDEDEDGDEVEEEAEPEYEEATERTTTSIATTTTTTTTSEVEEVVR-VPTTAASTP 297
        ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db      239 EEEADDD-DDDDGDETEEEPEEPYEEATERTTTSIATTTTTTTTSEVEEVVRVPATAVSTP 297
Qy      298 DAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVI 357
        ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db      298 DAVDKYLENPNDENEHDFLKAERLEGGHREKMSQVMREWEAAERQAKNLPKADKKAVI 357
Qy      358 QHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFN 417
        ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db      358 QHFQEKVESLEQEAAKERQQLVETHMARVEATLNDRRLALENYITALQADPPRPRHVFN 417
Qy      418 MLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVP 477
        ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db      418 MLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVINERMNQSFSLLYKVP 477
Qy      478 AVAEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGE 537
        ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db      478 AVAEIQDEVDELQKEQNYSDVMVSNMVSDFRVSYGNDAIMPSTETKTTVELLPVDGE 537
Qy      538 FSLDDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNL 597
        ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db      538 FNVDELQPWHSFGVDSVPANTENEVEPVDARPAADRGLTTRPGSGLTNIKREEISEVKMD 597
Qy      598 AEFRHDSGYEVHHQKLTVFFAEVGSNGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIH 657
        ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db      598 SEYRHDAAYEVHHQKLTVFFAEVGSNGAIIGLMVGGVVIATVIVITLVMLKKKQYTTIH 657
Qy      658 HGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695
        ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db      658 HGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695

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# RESULT 6

Q91963

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ID   Q91963      PRELIMINARY;      PRT;      747 AA.
AC   Q91963;
DT   01-NOV-1996 (TrEMBLrel. 01, Created)
DT   01-NOV-1996 (TrEMBLrel. 01, Last sequence update)
DT   01-JUN-2003 (TrEMBLrel. 24, Last annotation update)
DE   APP747.
GN   APP747.
OS   Xenopus.
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Amphibia; Batrachia; Anura; Mesobatrachia; Pipoidae; Pipidae;
OC   Xenopodinae.
OX   NCBI_TaxID=8353;
RN   [1]
RP   SEQUENCE FROM N.A.
RX   MEDLINE=93129227; PubMed=1282805;

```

RA Okado H., Okamoto H.;  
 RT "A Xenopus homologue of the human beta-amyloid precursor protein:  
 RT developmental regulation of its gene expression.";  
 RL Biochem. Biophys. Res. Commun. 189:1561-1568(1992).  
 DR EMBL; S52417; AAB24853.1; -.  
 DR HSSP; P05067; 1HZ3.  
 DR GO; GO:0016020; C:membrane; IEA.  
 DR GO; GO:0004867; F:serine protease inhibitor activity; IEA.  
 DR InterPro; IPR008155; A4\_APP.  
 DR InterPro; IPR008154; A4\_extra.  
 DR InterPro; IPR001255; Beta-APP.  
 DR InterPro; IPR002223; Kunitz\_BPTI.  
 DR Pfam; PF02177; A4\_EXTRA; 1.  
 DR Pfam; PF03494; Beta-APP; 1.  
 DR Pfam; PF00014; Kunitz\_BPTI; 1.  
 DR PRINTS; PR00203; AMYLOIDA4.  
 DR PRINTS; PR00759; BASICPTASE.  
 DR ProDom; PD000222; Kunitz\_BPTI; 1.  
 DR SMART; SM00131; KU; 1.  
 DR PROSITE; PS00319; A4\_EXTRA; 1.  
 DR PROSITE; PS00320; A4\_INTRA; 1.  
 DR PROSITE; PS00280; BPTI\_KUNITZ\_1; 1.  
 DR PROSITE; PS50279; BPTI\_KUNITZ\_2; 1.  
 KW Protease inhibitor; Serine protease inhibitor.  
 SQ SEQUENCE 747 AA; 84893 MW; A75E81885681D948 CRC64;

Query Match 84.8%; Score 3095; DB 13; Length 747;  
 Best Local Similarity 80.8%; Pred. No. 1.1e-177;  
 Matches 596; Conservative 36; Mismatches 42; Indels 64; Gaps 5;

Qy	17	ALEVPTDGNAGLLAEPQIAMF-CGRLNMHMNVQNGKWSDPSGKTCTCIDTKEGILQYCQE	75
		:	
Db	15	ALEVLVDGNGLLAEPQIAMFSVARLNMHMNVQNGKWETDVSG---CIGTKEGILQYCQE	71
Qy	76	VYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVGEFVSDALLVPDKCKF	135
		:     :    :	
Db	72	VYPELQITNVVEANQPVTIQNWCKKGRKQCKSRTHIVVPYRCLVGEFVSDALLVPDKCKF	131
Qy	136	LHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFRGVEFVCCPLAEESDN	195
		:       :     : : :       :     :	
Db	132	LHQERMDICETHLHWHTVAKESCSKSMLEHYGMLLPCGIDKFRGVEFVCCPSAEES	191
Qy	196	VDSADAEEDSDVWVGADTDYADGSEDKVVEVA---EEEEVAEVEEEEADDDDEDGDE	253
		:	
Db	192	FDSADAAEDDCDVWVGADADYVDRSDDKAVEAQPDEEEVVEVEEEEETDDDED--DGDE	249
Qy	254	VEEEAEEPVEEATERTTSIATTTTTTTTESVEEVVR-----	288
Db	250	AEEPEEPVEEATERTTSIATTTTTTTTESVEEVVREVCSEQAETGPCRAMISRWYYDVTE	309
Qy	289	-----VPTTAASTPDAVDKYLETPGDENEHAHFQ	317
		:	
Db	310	SKCAQFIYGGCGGNRNNFESDDYCMVCGSVIPATAASTPDAVDKYLENPNDENEHDFL	369
Qy	318	KAKERLEAKHRERMSQVMREWEAERQAKNLPKADKKAVIQHFQEKVESLEQEAANERQQ	377
		: : : : : : : : : : : : : : : : :	
Db	370	KAKERLEGKHREKMSEVMKEWEAERQAKNLPKADKKAVIQHFQEKVESLEQEAQQRQQ	429

Qy 378 LVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHf 437  
 |||||:|||||  
 Db 430 LVETHMARVEAMLNDRRIAENYITALQADPPRPRHVFNMLKKYVRAEQKDRQHTLKHf 489  
 Qy 438 EHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAVAEEIQDEVDELLQKEQNY 497  
 |||||:|||||  
 Db 490 EHVRMVDPKKAAQIRSQVMTHLRVINERMNQSFSLLYKVPAAVEEQDEVDELFOKEQNY 549  
 Qy 498 SDDVLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSLDDLQPWHSFGADSVPAN 557  
 |||::||:|:|:|||||:|||||:||:|:|:|:|:|  
 Db 550 SDDMVSNMVSDHRVSYGNDALMPSLSETKTTVELLPVDGEFNIEDLQPWHSFGVDSVPAN 609  
 Qy 558 TENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLDAEFRHDSGYEVHHQKLFFFA 617  
 |||||:|:|:|:|:|:|  
 Db 610 TENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDSEYRHDTAYEVHHQKLFFFA 669  
 Qy 618 EDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGVEVDAAVTPEERHLSKM 677  
 |:|||||:|||||:|||||:|  
 Db 670 EEVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTTIHGVEVDAAVTPEERHLTKM 729  
 Qy 678 QQNGYENPTYKFFEQMQN 695  
 |||||  
 Db 730 QQNGYENPTYKFFEQMQN 747

RESULT 7

O57394

ID O57394 PRELIMINARY; PRT; 699 AA.  
 AC O57394;  
 DT 01-JUN-1998 (TrEMBLrel. 06, Created)  
 DT 01-JUN-1998 (TrEMBLrel. 06, Last sequence update)  
 DT 01-JUN-2003 (TrEMBLrel. 24, Last annotation update)  
 DE EL amyloid precursor protein 699.  
 GN EL APP699.  
 OS Narke japonica (Electric ray).  
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Chondrichthyes;  
 OC Elasmobranchii; Squalia; Hymenoptera; Pristigasteria; Batoidea;  
 OC Torpediniformes; Narcinoidei; Narcidae; Narke.  
 OX NCBI\_TaxID=62965;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RC TISSUE=Electric lobe;  
 RX MEDLINE=98129705; PubMed=9461486;  
 RA Iijima K., Lee D.-S., Okutsu J., Tomita S., Hirashima N., Kirino Y.,  
 RA Suzuki T.;  
 RT "cDNA isolation of Alzheimer's amyloid precursor protein from  
 RT cholinergic nerve terminals of the electric organ of the electric  
 RT ray.";  
 RL Biochem. J. 330:29-33(1998).  
 DR EMBL; AB005544; BAA24230.1; -.  
 DR HSSP; P05067; 1HZ3.  
 DR GO; GO:0016020; C:membrane; IEA.  
 DR InterPro; IPR008155; A4\_APP.  
 DR InterPro; IPR008154; A4\_extra.  
 DR InterPro; IPR001255; Beta-APP.  
 DR Pfam; PF02177; A4\_EXTRA; 1.



Q9PVL1

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ID      Q9PVL1          PRELIMINARY;          PRT;    569 AA.
AC      Q9PVL1;
DT      01-MAY-2000 (TrEMBLrel. 13, Created)
DT      01-MAY-2000 (TrEMBLrel. 13, Last sequence update)
DT      01-JUN-2003 (TrEMBLrel. 24, Last annotation update)
DE      Amyloid protein (Fragment).
GN      APP.
OS      Gallus gallus (Chicken).
OC      Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC      Archosauria; Aves; Neognathae; Galliformes; Phasianidae; Phasianinae;
OC      Gallus.
OX      NCBI_TaxID=9031;
RN      [1]
RP      SEQUENCE FROM N.A.
RC      TISSUE=Brain;
RA      Coulson E.J., Paliga K., Beyreuther K., Masters C.L.;
RT      "What the evolution of the amyloid protein precursor supergene family
RT      tells us about its function.";
RL      Neurochem. Int. 0:0-0(2000).
DR      EMBL; AF030341; AAF12698.1; -.
DR      HSSP; P05067; 1BA4.
DR      GO; GO:0016020; C:membrane; IEA.
DR      InterPro; IPR008155; A4_APP.
DR      InterPro; IPR008154; A4_extra.
DR      InterPro; IPR001255; Beta-APP.
DR      Pfam; PF02177; A4_EXTRA; 1.
DR      Pfam; PF03494; Beta-APP; 1.
DR      PRINTS; PR00203; AMYLOIDA4.
DR      PROSITE; PS00319; A4_EXTRA; 1.
DR      PROSITE; PS00320; A4_INTRA; 1.
FT      NON_TER          1          1
SQ      SEQUENCE    569 AA;  64753 MW;  0AB8BB851863A19D CRC64;

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Query Match 75.6%; Score 2759.5; DB 13; Length 569;  
Best Local Similarity 93.2%; Pred. No. 1.1e-157;  
Matches 533; Conservative 15; Mismatches 19; Indels 5; Gaps 4;

Qy	126	ALLVDPDKCKFLHQERMDVCE	THLHWHTVAKETCSEKSTNL	HDYGMLLPCGIDKFRGVEFV	185
Db	1	ALLVDPDKCKLLHQERMDVCE	THLHWHTVAKESCSEKSMNL	HDYGMLLSCGIDKFRGVEFV	60
Qy	186	CCPLAEESDNVDSADAEEDD	SDVWVG	GADTDYADGSEDKVVE--VA	243
Db	61	CCPLAEESDNLDSADAEEDD	SDVWVG	GADADYADGSDDKVVEEQPE	120
Qy	244	DDEDDGDEVEEEAE	EPYEEATERTTSIATTTTTT	TESVEEVVRVPTTAASTPD	303
Db	121	DD-DDDDGDEI-EETEE	EYEEATERTTSIATTTTTT	TESVEEVVRVPTTAASTPD	178
Qy	304	LETPGDENEHAHFQKAK	ERLEAKHRERMSQVMREWE	EAEERQAKNLPKADKKAVI	363
Db	179	LETPGDENEHAHFQKAK	ERLEAKHRERMSQVMREWE	EAEERQAKNLPKADKKAVI	238



Qy 364 VESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLKKYV 423  
 |||||:|||||  
 Db 239 VESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQTVPPRPRHVFNMLKKYV 298

Qy 424 RAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAAVEEI 483  
 |||||:|||||  
 Db 299 RAEQKDRQHTLKHFEHVRMVDPKKAVQIRSQVMTHLRVIYERMNQSLSLLYNVPAAVEEI 358

Qy 484 QDEVDELLQKEQNYSDVLNMISEPRISYGNDALMPSLTETKTTVELLPVNGEFLDDL 543  
 |||||:|||||  
 Db 359 QDEVDELLQKEQNYSDVLNMISEPRISYGNDALMPTLTETKTTVELLPVNGEFLDDL 418

Qy 544 QPWSHFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLDAEFRHD 603  
 |||||:|||:|  
 Db 419 QPWHFPFGVDSVPANTENEVEPVDARPAADRGLTTRPGSGLTNVKTTEEVESEVKMDAEFRHD 478

Qy 604 SGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGHVVEV 663  
 |||||:|||||  
 Db 479 SGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIANVIVITLVMLKKKQYTSIHGHVVEV 538

Qy 664 DAAVTPEERHLSKMQQNGYENPTYKFFEQQMN 695  
 |||||  
 Db 539 DAAVTP-ERHLSKMQQNGYENPTYKFFEQQMN 569

RESULT 9

O93296

ID O93296 PRELIMINARY; PRT; 534 AA.  
 AC O93296;  
 DT 01-NOV-1998 (TrEMBLrel. 08, Created)  
 DT 01-NOV-1998 (TrEMBLrel. 08, Last sequence update)  
 DT 01-JUN-2003 (TrEMBLrel. 24, Last annotation update)  
 DE Amyloid protein (Fragment).  
 OS Gallus gallus (Chicken).  
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
 OC Archosauria; Aves; Neognathae; Galliformes; Phasianidae; Phasianinae;  
 OC Gallus.  
 OX NCBI\_TaxID=9031;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RX MEDLINE=98337885; PubMed=9671674;  
 RA Barnes N.Y., Li L., Yoshikawa K., Schwartz L.M., Oppenheim R.W.,  
 RA Milligan C.E.;  
 RT "Increased production of amyloid precursor protein provides a  
 RT substrate for caspase-3 in dying motoneurons."  
 RL J. Neurosci. 18:5869-5880(1998).  
 DR EMBL; AF042098; AAC25052.1; -.  
 DR HSSP; P05067; 1BA4.  
 DR GO; GO:0016020; C:membrane; IEA.  
 DR InterPro; IPR008155; A4\_APP.  
 DR InterPro; IPR008154; A4\_extra.  
 DR InterPro; IPR001255; Beta-APP.  
 DR Pfam; PF02177; A4\_EXTRA; 1.  
 DR Pfam; PF03494; Beta-APP; 1.  
 DR PRINTS; PR00203; AMYLOIDA4.  
 DR PROSITE; PS00319; A4\_EXTRA; 1.

DR PROSITE; PS00320; A4\_INTRA; 1.  
FT NON\_TER 1 1  
SQ SEQUENCE 534 AA; 60597 MW; FB53ECC2E66D4C92 CRC64;

Query Match 71.4%; Score 2605; DB 13; Length 534;  
Best Local Similarity 94.4%; Pred. No. 2e-148;  
Matches 504; Conservative 14; Mismatches 12; Indels 4; Gaps 3;

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Qy      164 NLHDYGMLLPCGIDKFRGVEFVCCPLAEESDNVDSADAEEEDSDVWVGADTDYADGSED 223
          |||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:
Db      3  NLHDYGMLLPCGIDKFRGVEFVCCPLAEESDNLDSADAEDDDSDVWVGADADYADGSDD 62

Qy      224 KVVE--VAEEEEVAEVEEEEADDDDEDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTE 281
          |||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:
Db      63 KVVEEQPEEDEELTVVEDEDADDD-DDDDGDEI-EETEEYEEATERTTSIATTTTTTTE 120

Qy      282 SVEEVVRVPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEA 341
          |||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:
Db      121 SVEEVVRVPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEA 180

Qy      342 ERQAKNLPKADKKAVIQHFQEKVESLEQEANERQQLVETHMARVEAMLNDRRRLALENY 401
          |||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:
Db      181 ERQAKNLPKADKKAVIQHFQEKVESLEQEANERQQLVETHMARVEAMLNDRRRIALENY 240

Qy      402 ITALQAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRV 461
          |||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:
Db      241 ITALQTVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRV 300

Qy      462 IYERMNQSLSLLYNVPAVAEEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPS 521
          |||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:
Db      301 IYERMNQSLSFLYNVPAVAEEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPS 360

Qy      522 LTETKTTVELLPVNGEFSDDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGS 581
          |||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:
Db      361 LTETKTTVELLPVDGEFSDDLQPWHPFGVDSVPANTENEVEPV DARPAADRGLTTRPGS 420

Qy      582 GLTNIKTEEISEVNLD AEFRHDSGYEVHHQKL VFFAEDVGSNKGAI IGLMVGGVVIATVI 641
          |||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:
Db      421 GLTNVKTEEVS EVKMD AEFRHDSGYEVHHQKL VFFAEDVGSNKGAI IGLMVGGVVIATVI 480

Qy      642 VITLVMLKKKQYTSIH HGVVEVDA AVTPEERHLSKMQQNGYENPTYKFFEQMQN 695
          |||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:
Db      481 VITLVMLKKKQYTSIH HGVVEVDA AVTPEERHLSKMQQNGYENPTYKFFEQMQN 534
```

RESULT 10

Q7ZZT1

ID Q7ZZT1 PRELIMINARY; PRT; 678 AA.  
AC Q7ZZT1;  
DT 01-JUN-2003 (TrEMBLrel. 24, Created)  
DT 01-JUN-2003 (TrEMBLrel. 24, Last sequence update)  
DT 01-OCT-2003 (TrEMBLrel. 25, Last annotation update)  
DE Amyloid protein a variant 2.  
GN APPA.  
OS Brachydanio rerio (Zebrafish) (Danio rerio).  
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
OC Actinopterygii; Neopterygii; Teleostei; Ostariophysi; Cypriniformes;

OC Cyprinidae; Danio.  
 OX NCBI\_TaxID=7955;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RA Groth C., Lardelli M.;  
 RT "Investigation of zebrafish appa expression during embryogenesis.";  
 RL Submitted (APR-2003) to the EMBL/GenBank/DDBJ databases.  
 DR EMBL; AY271746; AAP22958.1; -.  
 DR GO; GO:0016020; C:membrane; IEA.  
 DR InterPro; IPR008155; A4\_APP.  
 DR InterPro; IPR008154; A4\_extra.  
 DR InterPro; IPR001255; Beta-APP.  
 DR Pfam; PF02177; A4\_EXTRA; 1.  
 DR Pfam; PF03494; Beta-APP; 1.  
 DR PRINTS; PR00203; AMYLOIDA4.  
 DR SMART; SM00006; A4\_EXTRA; 1.  
 DR PROSITE; PS00319; A4\_EXTRA; 1.  
 DR PROSITE; PS00320; A4\_INTRA; 1.  
 SQ SEQUENCE 678 AA; 76755 MW; 94163778444FD0BC CRC64;

Query Match 70.2%; Score 2562; DB 13; Length 678;  
 Best Local Similarity 71.9%; Pred. No. 1e-145;  
 Matches 498; Conservative 78; Mismatches 95; Indels 22; Gaps 11;

Qy	5	LALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGKTCTCID	64
		:  :  :   :  :	
Db	6	LFILLMAVASTLAVEVPSDGTGLLAEPQIAMFCGKLNMHINIQSGKWEPPDPSGSKSCIG	65
Qy	65	TKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVGEFVS	124
Db	66	NKEGILQYCQEVYPELQITNVVEANQPVSIWDWCKKSRKQCRSHMHIVVPYRCLVGEFVS	125
Qy	125	DALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFRGVEF	184
Db	126	DALLVPDKCKFLHQERMDMCESHLHWHTVAKESCGDRSMNLHDYGMLLPCGIDRFRGVEF	185
Qy	185	VCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEEEEEEADD	244
		: :                               :   :	
Db	186	VCCP-ADAGKESESA AVEEDSDVWVGGA EADYTENSMTR--DAAAEPV--LEDDEDAD	240
Qy	245	DEDDDEDGD-EVEEEAE EPYEEATERTT-SIATTTTTTTESVEEVVRVPTTAASTPDAVDK	302
		:   :         : :	
Db	241	EEEDDEDGDGRDEKIEEEEEERTQSTSAALTSTTTTTTESVEEVVRVPTPSSSPDAVDR	300
Qy	303	YLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHFQE	362
Db	301	YLETPADENEHAHFLKAKESLETKHRERMSQVMREWEAAERQAKSLPRNDKKAVIQHFQE	360
Qy	363	KVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLKKY	422
		:         :	
Db	361	KVEALEQESASERQQLVETHMARVEALLNDRRLALESYLSALQADPPRPRHVFSLLKKY	420
Qy	423	VRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAAVEE	482
Db	421	VRAEQKDRQHTLKHFEHVRMVDPKKAAQIRPQVLTHLRVIEERMNQSLGLLYKVPGVADD	480
Qy	483	IQDEVDELLQKEQNYSDDVLANMISEPRI SYGNDALMPSLTETKTTVELLPVNGEFSLDD	542

Db	481	IQDQV-ELLQREQQEMSAQLANLQSDARVSYGNDALMPDST---AGLELLPAEDTQGFGF	536
Qy	543	LQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLDAEFRH	602
Db	537	IHP-ESFN----QPNTHNQVEPVDARVPVPLDLATRPVSGL---KPDDIPELRMEAEERH	588
Qy	603	DSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGVVE	662
Db	589	S---EVYHQKLVFFAEDVSSNKGAIIGLMVGGVVIATIIVITLVMLRKKQYTSIHGGIIE	645
Qy	663	VDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN	695
Db	646	VDAAVTPEERHLSKMQQNGYENPTYKFFEQMHN	678

Q90W28

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ID      Q90W28          PRELIMINARY;          PRT;    738 AA.
AC      Q90W28;
DT      01-DEC-2001 (TrEMBLrel. 19, Created)
DT      01-DEC-2001 (TrEMBLrel. 19, Last sequence update)
DT      01-JUN-2003 (TrEMBLrel. 24, Last annotation update)
DE      Amyloid precursor protein.
GN      APPA OR APP.
OS      Brachydanio rerio (Zebrafish) (Danio rerio).
OC      Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC      Actinopterygii; Neopterygii; Teleostei; Ostariophysi; Cypriniformes;
OC      Cyprinidae; Danio.
OX      NCBI_TaxID=7955;
RN      [1]
RP      SEQUENCE FROM N.A.
RA      Groth C., Lardelli M.;
RT      "Expression analysis of zebrafish app.";
RL      Submitted (JUN-2001) to the EMBL/GenBank/DDBJ databases.
DR      EMBL; AF389401; AAK64495.1; -.
DR      ZFIN; ZDB-GENE-000616-13; appa.
DR      GO; GO:0016020; C:membrane; IEA.
DR      GO; GO:0004867; F:serine protease inhibitor activity; IEA.
DR      InterPro; IPR008155; A4_APP.
DR      InterPro; IPR008154; A4_extra.
DR      InterPro; IPR001255; Beta-APP.
DR      InterPro; IPR002223; Kunitz_BPTI.
DR      Pfam; PF02177; A4_EXTRA; 1.
DR      Pfam; PF03494; Beta-APP; 1.
DR      Pfam; PF00014; Kunitz_BPTI; 1.
DR      PRINTS; PR00203; AMYLOIDA4.
DR      PRINTS; PR00759; BASICPTASE.
DR      ProDom; PD000222; Kunitz_BPTI; 1.
DR      SMART; SM00006; A4_EXTRA; 1.
DR      SMART; SM00131; KU; 1.
DR      PROSITE; PS00319; A4_EXTRA; 1.
DR      PROSITE; PS00320; A4_INTRA; 1.
DR      PROSITE; PS00280; BPTI_KUNITZ_1; 1.
DR      PROSITE; PS50279; BPTI_KUNITZ_2; 1.
KW      Protease inhibitor; Serine protease inhibitor.
SQ      SEQUENCE      738 AA;  83577 MW;  AF480F6D308FD298 CRC64;

```

Query Match 69.1%; Score 2524; DB 13; Length 738;  
Best Local Similarity 66.3%; Pred. No. 2.2e-143;  
Matches 500; Conservative 79; Mismatches 91; Indels 84; Gaps 14;

```
Qy      5 LALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGKTCTCID 64
| :||:| : |:||:| | ||||| :|||:|:|:|:| :|||:|:|
Db      6 LFILLMAVASTLAVEVPSDSGTGLLAEPQIAMFCGKLMHINIQSGKWEPDPSGSKSCIG 65

Qy     65 TKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVGEFVS 124
| ||||| :|||:| ||||:| | |:|||||
Db     66 NKEGILQYCQEVYPELQITNVVEANQPVSIWDWCKKSRKQCRSHMHIVVPIYRCLVGEFVS 125

Qy    125 DALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFRGVEF 184
| ||||| :||:| |||||:| :| | |||||:| |||||
Db    126 DALLVPDKCKFLHQERMDMCESHLHWHTVAKESCGDRSMNLHDYGMLLPCGIDRFRGVEF 185

Qy    185 VCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEEEADD 244
| ||| |: :|| | ||||| :|| :| : :| | | :|:|:|
Db    186 VCCP-ADAGKESESAAVEEDDSVWVGAEADYTENSMT--DAAAEPAVLE-DDEDADE 241

Qy    245 DED-DEDGD-----EVEEEAEPEYEEATERTT-SIATTTTTTTESVEEVVR----- 288
: || |:|| :||| || || |: |: : :| |||||
Db    242 EEDEDQDGDGDRDEKIEEEEE--EERTQSTSAALTSTTTTTTESVEEVVREVCFASAET 299

Qy    289 -----VPTTAASTPDAVD 301
: || :| ||||
Db    300 GPCRAML SRWYYVREERRCAPFIYGGCGGNRNNFESEYCLSVCSGVLPTSSSPDAVD 359

Qy    302 KYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHFQ 361
: |||| | |||| | ||| || | ||||| :||: | |||||
Db    360 RYLETPADENEHAHFLKAKESLETKHRERMSQVMREWEAAERQAKSLPRNDKKAVIQHFQ 419

Qy    362 EKVESLEQEAAANERQQVLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLKK 421
| |||:| |||:| :||| :||| :||| :||| :||| :||| :|||
Db    420 EKVEALEQESASERQQVLVETHMARVEALLNDRRLALESYLSALQADPPRPRHVFSLKK 479

Qy    422 YVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAVAE 481
| ||||| :|||:| ||||| :|||:| ||||| :|||:| ||||| :|||:|
Db    480 YVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRPQVLTHLRVIEERMNQSGLLYKVPGVAD 539

Qy    482 EIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSLD 541
: |||:| |||:| |||:| |: |:| ||||| | :|||
Db    540 DIQDQV-ELLQREQQEMSAQLANLQSDARVSYGN DALMPDST---AGLELLPAEDTQGGFG 595

Qy    542 DLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEFR 601
: | || | | :||| | | | ||| | | :| |: :|| |
Db    596 FIHP-ESFN---QPNTHNQVEPVDARVPDLDLATRPVSGL---KPDDIPELRMEAEER 647

Qy    602 HDSGYEVVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIH HGVV 661
| | :||| :||| :||| :||| :||| :||| :||| :||| :|||
Db    648 HS---EVYHQKLVFFAEDVSSNKGAIIGLMVGGVVIATIIIVITLVMLRKKQYTSIH HGII 704

Qy    662 EVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QN 695
| ||||| :|||:| ||||| :|||:| ||||| :|||:|
Db    705 EVDAAVTPEERHLSKMQQNGYENPTYKFFEQM HN 738
```

# RESULT 12

Q8UUR9

ID Q8UUR9 PRELIMINARY; PRT; 694 AA.  
AC Q8UUR9;  
DT 01-MAR-2002 (TrEMBLrel. 20, Created)  
DT 01-MAR-2002 (TrEMBLrel. 20, Last sequence update)  
DT 01-JUN-2003 (TrEMBLrel. 24, Last annotation update)  
DE Putative membrane protein.  
GN APPB.  
OS Brachydanio rerio (Zebrafish) (Danio rerio).  
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
OC Actinopterygii; Neopterygii; Teleostei; Ostariophysi; Cypriniformes;  
OC Cyprinidae; Danio.  
OX NCBI\_TaxID=7955;  
RN [1]  
RP SEQUENCE FROM N.A.  
RC TISSUE=Brain;  
RX PubMed=11862463;  
RA Musa A., Lehrach H., Russo V.E.A.;  
RT "Distinct expression patterns of two zebrafish homologues of the human  
RT APP gene during embryonic development.";  
RL Dev. Genes Evol. 211:563-567(2001).  
DR EMBL; AJ315639; CAC85736.1; -.  
DR ZFIN; ZDB-GENE-020220-1; appb.  
DR GO; GO:0016020; C:membrane; IEA.  
DR InterPro; IPR008155; A4\_APP.  
DR InterPro; IPR008154; A4\_extra.  
DR InterPro; IPR001255; Beta-APP.  
DR Pfam; PF02177; A4\_EXTRA; 1.  
DR Pfam; PF03494; Beta-APP; 1.  
DR PRINTS; PR00203; AMYLOIDA4.  
DR SMART; SM00006; A4\_EXTRA; 1.  
DR PROSITE; PS00319; A4\_EXTRA; 1.  
DR PROSITE; PS00320; A4\_INTRA; 1.  
SQ SEQUENCE 694 AA; 79228 MW; 2B03382D411162DC CRC64;

Query Match 68.1%; Score 2487.5; DB 13; Length 694;  
Best Local Similarity 68.0%; Pred. No. 3.2e-141;  
Matches 478; Conservative 96; Mismatches 98; Indels 31; Gaps 9;

Qy 7 LLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGKTCTIDTK 66  
| | | : : | : | | : | : | | | | : | | | : | | | : | | : | | : | | | |  
Db 9 LLLMLTTLSLAIEVPSDDSVGLLAEPQVAMFCGKLNMHINVQSGKWEPTDPTGKSCISTK 68  
Qy 67 EGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVGEFVSDA 126  
| | | | : | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |  
Db 69 EGILKYCQEVYPDLQITNVVEANQPVSIQNWCKMGRRQCRSHTHIVVPYRCLVGEFVSDA 128  
Qy 127 LLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFRGVEFVC 186  
| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |  
Db 129 LLVPDKCKFLHQERMDMCESHLHWHTVAKESCGDRSMNLHDYGMLLPCGIDRFRGVEFVC 188  
Qy 187 CPLAEESDNVDSADAEEDSDVWVGADTDYADGS--EDKVV-----EVAEEEEVAEEVEE 239  
| | : | : | : | | : | | : | | | | | | | | | | | | | | | | | | | | | | | |  
Db 189 CPMEEQKD-LDSEEQEEANSDVWVGGAETEYTDASVLKEQVTAKPDPAVTEDEDLNEE 247



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DR      InterPro; IPR008154; A4_extra.
DR      InterPro; IPR001255; Beta-APP.
DR      Pfam; PF02177; A4_EXTRA; 1.
DR      Pfam; PF03494; Beta-APP; 1.
DR      PRINTS; PR00203; AMYLOIDA4.
DR      PROSITE; PS00319; A4_EXTRA; 1.
DR      PROSITE; PS00320; A4_INTRA; 1.
FT      NON_TER      1      1
SQ      SEQUENCE      612 AA; 69710 MW; 59A9ACBDF9C59EFF CRC64;

```

Qy	68	GILQYQCQEVYPQLQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVGEFVSDAL	127
Db	1	GILQYQCQEVYPQLQITNVVEANQPVSIWDWCKKSRKQCRSHMHIVVPIYRCLVGEFVSDAL	60
Qy	128	LVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFRGVEFVCC	187
Db	61	LVPDKCKFLHQERMDMCESHLHWHTVAKESCGDRSMNLHDYGMLLPCGIDRFRGVEFVCC	120
Qy	188	PLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEEEEEEADDDDED	247
Db	121	P-ADAGKESSESAAVEEDDSVWVGGAADYTENSMT--DAAAEPAV--LEDDADEEEE	175
Qy	248	DEDGD-----EVEEEAEPEYEEATERTT-SIATTTTTTTESVEEVVRVPTTAASTPDAVD	301
Db	176	DEDGDGDRDEKIEEEEE--EERTQSTSAALTSTTTTTTESVDEVVRVPTPSSSPDAVD	233
Qy	302	KYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHFQ	361
Db	234	RYLETPADENEHAHFLKAKESLETKHRERMSQVMREWEAAERQAKSLPRNDKKAVIQHFQ	293
Qy	362	EKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLKK	421
Db	294	EKVEALEQESASERQQLVETHMARVEALLNDRRLALESYLSALQADPPRPRHVFSLKK	353
Qy	422	YVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAAVE	481
Db	354	YVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRPQVLTHLRVIEERMNQSLGLLYKVPGVAD	413
Qy	482	EIQDEVDELLQKEQNYSDDLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFLSD	541
Db	414	DIQDQV-ELLQREQQEMSAQLANLQSDARVSYGNDALMPDST---AGLELLPAEDTQGFG	469
Qy	542	DLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLDAEFR	601
Db	470	FIHP-ESEF-----QPNTNHNQVEPVDARVPDLDLATRPVSGL---KPDDIPELRMEAEER	521
Qy	602	HDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMMLKKKQYTSIHHGVV	661
Db	522	HS---EVYHQKLVFFAEDVSSNKGAIIGLMVGGVVIATIIIVITLVMMLRKKQYTSIHHGII	578
Qy	662	EVDAAVTPEERHLSKMQQNGYENPTYKFFEOMQN	695
Db	579	EVDAAVTPEERHLSKMQQNGYENPTYKFFEOMHN	612



## O8BPC7

Query Match 52.6%; Score 1920; DB 11; Length 384;  
Best Local Similarity 97.7%; Pred. No. 1.8e-107;  
Matches 375; Conservative 3; Mismatches 6; Indels 0; Gaps 0;

Qy	312	EHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHFQEKVESLEQEA	371
Db	1	EHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHFQEKVESLEQEA	60
Qy	372	ANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPHVFNMLKKYVRAEQKDRQ	431
Db	61	ANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPHVFNMLKKYVRAEQKDRQ	120
Qy	432	HTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAAVEEIQDEVDELL	491
Db	121	HTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAAVEEIQDEVDELL	180
Qy	492	QKEQNYSDVDLANMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSLDDLQPWHSFGA	551
Db	181	QKEQNHSDDVLANMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSLDDLQPWHPFGV	240
Qy	552	DSVPANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLDAEFRHDSGYEVHHQ	611

Db 241 DSVPA NTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEFGHDSGFEVRHQ 300

Qy 612 KLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGVVEVDAAVTPEE 671  
 |||

Db 301 KLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGVVEVDAAVTPEE 360

Qy 672 RHL SKMQQNGYENPTYKFFEQMQN 695  
 |||

Db 361 RHL SKMQQNGYENPTYKFFEQMQN 384

RESULT 15

Q13861

ID Q13861 PRELIMINARY; PRT; 695 AA.

AC Q13861;

DT 01-NOV-1996 (TrEMBLrel. 01, Created)

DT 01-NOV-1996 (TrEMBLrel. 01, Last sequence update)

DT 01-JUN-2003 (TrEMBLrel. 24, Last annotation update)

DE Binding protein (Fragment).

OS Homo sapiens (Human).

OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;

OC Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.

OX NCBI\_TaxID=9606;

RN [1]

RP SEQUENCE FROM N.A.

RC TISSUE=Brain;

RA Vostrov A.A., Quitschke W.W., Schwarzman A.L., Blangy A., Cuzin F.,

RA Wesley U.V., Hagag N.G., Goldgaber D.;

RT "Cloning of a protein that binds to a recognition sequence in the APP

RT promoter.";

RL Submitted (JUN-1993) to the EMBL/GenBank/DDBJ databases.

DR EMBL; L19597; AAA35601.1; -.

DR HSSP; P05067; 1MWP.

DR InterPro; IPR008155; A4\_APP.

DR InterPro; IPR008154; A4\_extra.

DR Pfam; PF02177; A4\_EXTRA; 1.

DR PRINTS; PR00203; AMYLOIDA4.

DR SMART; SM00006; A4\_EXTRA; 1.

DR PROSITE; PS00319; A4\_EXTRA; 1.

DR PROSITE; PS00320; A4\_INTRA; 1.

FT NON\_TER 1 1

FT NON\_TER 695 695

SQ SEQUENCE 695 AA; 79238 MW; 728CA8ACBB7594FB CRC64;

Query Match 48.3%; Score 1762; DB 4; Length 695;

Best Local Similarity 50.8%; Pred. No. 1.2e-97;

Matches 366; Conservative 113; Mismatches 171; Indels 70; Gaps 17;

Qy 5 LALLLLAAWTARALEV-----PTDGNAG---LLAEPQIAMFCGRLNMHMNVQNGKWSDP 56  
 | ||| ||| : ||| : ||| ||| : ||| : ||| : ||| : ||| : |||

Db 15 LLLLLLVGLTAPALALAGYIEALAANAGTGFAVAEPQIAMFCGKLNMHVNIQTGKWE PDP 74

Qy 57 SGTKTCTIDTKEGILQYCYQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYR 116  
 : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : |||

Db 75 TGTKSCFETKEEVLYCYQEMYPELQITNVMEANQRVSIDNWCRRDKKQCKS--RFVTPFK 132

Qy 117 CLVGEFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGI 176

Db	133	CLVGEFVSDVLLVPEKQCFHKERMEVCENHQHWHTVVKEACLTQGMTLYSYGMLLPCGV	192
Qy	177	DKFRGVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAE	236
Db	193	DQFHGTEYVCCPQTKIIGSVSKEEEEEDEE-----EEEEDEEEDYDVYKSEFPTEAD	245
Qy	237	VEE--EEA--DDDEDDDEDGDEVEEEAE-----EPYEEATERTTSIATTTTTTTESVE	284
Db	246	LEDFTAAVDEDEDEEEGEEVVEDRDYYYDTFKGDDYNE--ENPTEPGSDGTMSDKEIT	303
Qy	285	EVVRVPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQ	344
Db	304	HDVKVPPTPLPTND-VDVYFETSADDNEHARFQKAKEQLEIRHRNRMDRVKKEWEEAELQ	362
Qy	345	AKNLPKADKKAVIQHFQEKVESLEQEAAANERQQLVETHMARVEAMLNDRRRLALENYITA	404
Db	363	AKNLPKAERQTLIQHFQAMVKALEKEAASEKQQLVETHLARVEAMLNDRRRMALENYLAA	422
Qy	405	LQAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYE	464
Db	423	LQSDPFRPHRILQALRRYVRAENKDLRHTIRHYQHVLAVDPEKAAQMKSQVMTHLHVIEE	482
Qy	465	RMNQSLSLLYNVPAAVEEIQDEVELLQKEQNYSDVLANMISEPRISYGNDAIMPSTLITE	524
Db	483	RRNQSLSLLYKVPYVAQEIQEEIDELLQEQR-----ADM-----DQFTASISE	525
Qy	525	TKTTVELLPVNGEFSLDDLQPWHSFGADSVANTENEVEPVDPARPAADRGL-----	575
Db	526	TPVDVR---VSSEES-EEIPPFHPF--HPFPALPENEGSGVGEQ---DGGLIGAEKVIN	576
Qy	576	-TTRPGSGLTNIKTEEISEVNLDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGG	634
Db	577	SKNKVDENMVIDETLDVKEMI FNAE--RVGGLEERESVGPLREDFSLSSSALIGLLVIA	634
Qy	635	VVIATVIVITLVMLKKKQYTSIHGVEVDAAVTPEERHLSKMQONGYENPTYKFFEQMQ	694
Db	635	VAIATVIVISLVMLRKROYGTISHGIVEVDPMLTPEERHLNKMQNHYENPTYKYLEQMQ	694

Search completed: July 26, 2004, 12:46:34  
Job time : 36.3333 secs

OM protein - protein search, using sw model

Run on: July 26, 2004, 12:39:28 ; Search time 9 Seconds  
(without alignments)  
4032.544 Million cell updates/sec

Title: US-09-806-194A-18  
Perfect score: 3651  
Sequence: 1 MLPGLALLLLAAWTARALEV.....QQNGYENPTYKFFEQMQNKK 697

Scoring table: BLOSUM62  
Gapop 10.0 , Gapext 0.5

Searched: 141681 seqs, 52070155 residues

Total number of hits satisfying chosen parameters: 141681

Minimum DB seq length: 0  
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%  
Maximum Match 100%  
Listing first 45 summaries

Database : SwissProt\_42:\*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

# SUMMARIES

Result No.	Score	Query		DB	ID	Description
		Match	Length			
1	3582.5	98.1	770	1	A4_HUMAN	P05067 h amyloid b
2	3582.5	98.1	770	1	A4_MACFA	P53601 m amyloid b
3	3576	97.9	751	1	A4_SAISC	Q95241 s amyloid b
4	3527.5	96.6	770	1	A4_PIG	P79307 s amyloid b
5	3514.5	96.3	770	1	A4_CAVPO	Q60495 c amyloid b
6	3485.5	95.5	770	1	A4_MOUSE	P12023 m amyloid b
7	3485.5	95.5	770	1	A4_RAT	P08592 r amyloid b
8	2568	70.3	780	1	A4_TETFL	O73683 tetraodon f
9	2446.5	67.0	737	1	A4_FUGRU	O93279 fugu rubrip
10	1730	47.4	695	1	APP2_MOUSE	Q06335 mus musculu
11	1725	47.2	763	1	APP2_HUMAN	Q06481 homo sapien
12	1709	46.8	765	1	APP2_RAT	P15943 rattus norv
13	1191	32.6	650	1	APP1_HUMAN	P51693 homo sapien
14	1183	32.4	653	1	APP1_MOUSE	Q03157 mus musculu
15	815.5	22.3	686	1	A4_CAEEL	Q10651 caenorhabdi
16	747.5	20.5	887	1	A4_DROME	P14599 drosophila
17	284	7.8	59	1	A4_BOVIN	Q28053 bos taurus

18	280	7.7	58	1	A4_RABIT	Q28748	oryctolagus
19	280	7.7	58	1	A4_SHEEP	Q28757	ovis aries
20	279	7.6	58	1	A4_CANFA	Q28280	canis famil
21	275	7.5	57	1	A4_URUMA	Q29149	ursus marit
22	185.5	5.1	407	1	IE68_HSVSA	Q01042	herpesvirus
23	185.5	5.1	993	1	SCP1_MOUSE	Q62209	mus musculu
24	176	4.8	2004	1	MYS3_HUMAN	Q92794	homo sapien
25	175.5	4.8	802	1	NAB3_YEAST	P38996	saccharomyc
26	171.5	4.7	793	1	CALD_HUMAN	Q05682	homo sapien
27	170	4.7	1498	1	GOA3_HUMAN	Q08378	homo sapien
28	169.5	4.6	297	1	TRT2_HUMAN	P45379	homo sapien
29	169.5	4.6	1875	1	MLP1_YEAST	Q02455	saccharomyc
30	169	4.6	771	1	CALD_CHICK	P12957	gallus gall
31	168	4.6	721	1	YCF2_OENPI	P31568	oenothera p
32	167.5	4.6	816	1	YG3A_YEAST	P53278	saccharomyc
33	167	4.6	1240	1	YNJ1_YEAST	P53935	saccharomyc
34	166.5	4.6	681	1	MP10_HUMAN	O00566	homo sapien
35	164	4.5	2017	1	MYSN_DROME	Q99323	drosophila
36	163.5	4.5	1976	1	MYHA_HUMAN	P35580	homo sapien
37	162.5	4.5	712	1	NUCL_RAT	P13383	rattus norv
38	162.5	4.5	1332	1	SPT7_YEAST	P35177	saccharomyc
39	162.5	4.5	1447	1	GOA3_MOUSE	P55937	mus musculu
40	161.5	4.4	1976	1	MYHA_RAT	Q9jlt0	rattus norv
41	160.5	4.4	1955	1	PUMA_PARUN	O61308	parascaris
42	158	4.3	301	1	TRT2_CHICK	P02642	gallus gall
43	157.5	4.3	1976	1	MYHA_BOVIN	Q27991	bos taurus
44	157	4.3	706	1	NUCL_HUMAN	P19338	homo sapien
45	156.5	4.3	5596	1	MDN1_HUMAN	Q9nu22	homo sapien

# ALIGNMENTS

## RESULT 1

### A4\_HUMAN

ID A4\_HUMAN STANDARD; PRT; 770 AA.

AC P05067; P09000; P78438; Q13764; Q13778; Q13793; Q16011; Q16014;

AC Q16019; Q16020; Q9BT38; Q9UCA9; Q9UCB6; Q9UCC8; Q9UCD1; Q9UQ58;

DT 13-AUG-1987 (Rel. 05, Created)

DT 01-NOV-1991 (Rel. 20, Last sequence update)

DT 15-MAR-2004 (Rel. 43, Last annotation update)

DE Amyloid beta A4 protein precursor (APP) (ABPP) (Alzheimer's disease

DE amyloid protein) (Cerebral vascular amyloid peptide) (CVAP) (Protease

DE nexin-II) (PN-II) (APPI) (PreA4) [Contains: Soluble APP-alpha (S-APP-

DE alpha); Soluble APP-beta (S-APP-beta); C99; Beta-amyloid protein 42

DE (Beta-APP42); Beta-amyloid protein 40 (Beta-APP40); C83; P3(42);

DE P3(40); Gamma-CTF(59) (Gamma-secretase C-terminal fragment 59)

DE (Amyloid intracellular domain 59) (AID(59)); Gamma-CTF(57) (Gamma-

DE secretase C-terminal fragment 57) (Amyloid intracellular domain 57)

DE (AID(57)); Gamma-CTF(50) (Gamma-secretase C-terminal fragment 50)

DE (Amyloid intracellular domain 50) (AID(50)); C31].

GN APP OR A4 OR AD1.

OS Homo sapiens (Human).

OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;

OC Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.

OX NCBI\_TaxID=9606;

RN [1]

RP SEQUENCE FROM N.A. (ISOFORM APP695).  
 RC TISSUE=Brain;  
 RX MEDLINE=87144572; PubMed=2881207;  
 RA Kang J., Lemaire H.-G., Unterbeck A., Salbaum J.M., Masters C.L.,  
 RA Grzeschik K.-H., Multhaup G., Beyreuther K., Mueller-Hill B.;  
 RT "The precursor of Alzheimer's disease amyloid A4 protein resembles a  
 RT cell-surface receptor.";  
 RL Nature 325:733-736(1987).  
 RN [2]

RP SEQUENCE FROM N.A. (ISOFORM APP751).  
 RC TISSUE=Brain;  
 RX MEDLINE=88122639; PubMed=2893289;  
 RA Ponte P., Gonzalez-Dewhitt P., Schilling J., Miller J., Hsu D.,  
 RA Greenberg B., Davis K., Wallace W., Lieberburg I., Fuller F.,  
 RA Cordell B.;  
 RT "A new A4 amyloid mRNA contains a domain homologous to serine  
 RT proteinase inhibitors.";  
 RL Nature 331:525-527(1988).  
 RN [3]

RP SEQUENCE FROM N.A. (ISOFORM APP695).  
 RX MEDLINE=89128427; PubMed=2783775;  
 RA Lemaire H.-G., Salbaum J.M., Multhaup G., Kang J., Bayney R.M.,  
 RA Unterbeck A., Beyreuther K., Mueller-Hill B.;  
 RT "The PreA4(695) precursor protein of Alzheimer's disease A4 amyloid  
 RT is encoded by 16 exons.";  
 RL Nucleic Acids Res. 17:517-522(1989).  
 RN [4]

RP SEQUENCE FROM N.A. (ISOFORM APP770).  
 RX MEDLINE=90236318; PubMed=2110105;  
 RA Yoshikai S.-I., Sasaki H., Doh-Ura K., Furuya H., Sakaki Y.;  
 RT "Genomic organization of the human amyloid beta-protein precursor  
 RT gene.";  
 RL Gene 87:257-263(1990).  
 RN [5]

RP ERRATUM, AND REVISIONS.  
 RA Yoshikai S.-I., Sasaki H., Doh-ura K., Furuya H., Sakaki Y.;  
 RL Gene 102:291-292(1991).  
 RN [6]

RP SEQUENCE FROM N.A. (ISOFORM L-APP733).  
 RC TISSUE=Leukocyte;  
 RX MEDLINE=92268136; PubMed=1587857;  
 RA Koenig G., Moenning U., Czech C., Prior R., Banati R.,  
 RA Schreiter-Gasser U., Bauer J., Masters C.L., Beyreuther K.;  
 RT "Identification and differential expression of a novel alternative  
 RT splice isoform of the beta A4 amyloid precursor protein (APP) mRNA in  
 RT leukocytes and brain microglial cells.";  
 RL J. Biol. Chem. 267:10804-10809(1992).  
 RN [7]

RP SEQUENCE FROM N.A. (ISOFORM APP770).  
 RX MEDLINE=97263807; PubMed=9108164;  
 RA Hattori M., Tsukahara F., Furuhashi Y., Tanahashi H., Hirose M.,  
 RA Saito M., Tsukuni S., Sakaki Y.;  
 RT "A novel method for making nested deletions and its application for  
 RT sequencing of a 300 kb region of human APP locus.";  
 RL Nucleic Acids Res. 25:1802-1808(1997).  
 RN [8]

RP SEQUENCE FROM N.A. (ISOFORM APP639).

RC TISSUE=Brain;  
 RX MEDLINE=22744650; PubMed=12859342;  
 RA Tang K., Wang C., Shen C., Sheng S., Ravid R., Jing N.;  
 RT "Identification of a novel alternative splicing isoform of human  
 RT amyloid precursor protein gene, APP639.";  
 RL Eur. J. Neurosci. 18:102-108(2003).  
 RN [9]  
 RP SEQUENCE FROM N.A. (ISOFORM APP305).  
 RC TISSUE=Pancreas;  
 RX MEDLINE=22388257; PubMed=12477932;  
 RA Strausberg R.L., Feingold E.A., Grouse L.H., Derge J.G.,  
 RA Klausner R.D., Collins F.S., Wagner L., Shenmen C.M., Schuler G.D.,  
 RA Altschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., Bhat N.K.,  
 RA Hopkins R.F., Jordan H., Moore T., Max S.I., Wang J., Hsieh F.,  
 RA Diatchenko L., Marusina K., Farmer A.A., Rubin G.M., Hong L.,  
 RA Stapleton M., Soares M.B., Bonaldo M.F., Casavant T.L., Scheetz T.E.,  
 RA Brownstein M.J., Usdin T.B., Toshiyuki S., Carninci P., Prange C.,  
 RA Raha S.S., Loquellano N.A., Peters G.J., Abramson R.D., Mullahy S.J.,  
 RA Bosak S.A., McEwan P.J., McKernan K.J., Malek J.A., Gunaratne P.H.,  
 RA Richards S., Worley K.C., Hale S., Garcia A.M., Gay L.J., Hulyk S.W.,  
 RA Villalon D.K., Muzny D.M., Sodergren E.J., Lu X., Gibbs R.A.,  
 RA Fahey J., Helton E., Kettelman M., Madan A., Rodrigues S., Sanchez A.,  
 RA Whiting M., Madan A., Young A.C., Shevchenko Y., Bouffard G.G.,  
 RA Blakesley R.W., Touchman J.W., Green E.D., Dickson M.C.,  
 RA Rodriguez A.C., Grimwood J., Schmutz J., Myers R.M.,  
 RA Butterfield Y.S.N., Krzywinski M.I., Skalska U., Smailus D.E.,  
 RA Schnerch A., Schein J.E., Jones S.J.M., Marra M.A.;  
 RT "Generation and initial analysis of more than 15,000 full-length  
 RT human and mouse cDNA sequences.";  
 RL Proc. Natl. Acad. Sci. U.S.A. 99:16899-16903(2002).  
 RN [10]  
 RP SEQUENCE OF 1-10 FROM N.A.  
 RC TISSUE=Liver;  
 RX MEDLINE=89016647; PubMed=3140222;  
 RA Schon E.A., Mita S., Sadlock J., Herbert J.;  
 RT "A cDNA specifying the human amyloid beta precursor protein (ABPP)  
 RT encodes a 95-kDa polypeptide.";  
 RL Nucleic Acids Res. 16:9351-9351(1988).  
 RN [11]  
 RP ERRATUM, AND REVISIONS.  
 RA Mita S., Sadlock J., Herbert J., Schon E.A.;  
 RL Nucleic Acids Res. 16:11402-11402(1988).  
 RN [12]  
 RP SEQUENCE OF 1-75 FROM N.A.  
 RX MEDLINE=89165870; PubMed=2538123;  
 RA La Fauci G., Lahiri D.K., Salton S.R., Robakis N.K.;  
 RT "Characterization of the 5'-end region and the first two exons of the  
 RT beta-protein precursor gene.";  
 RL Biochem. Biophys. Res. Commun. 159:297-304(1989).  
 RN [13]  
 RP SEQUENCE OF 18-50.  
 RC TISSUE=Fibroblast;  
 RX MEDLINE=87250462; PubMed=3597385;  
 RA van Nostrand W.E., Cunningham D.D.;  
 RT "Purification of protease nexin II from human fibroblasts.";  
 RL J. Biol. Chem. 262:8508-8514(1987).  
 RN [14]

RP PARTIAL SEQUENCE FROM N.A. (ISOFORM APP751).  
 RC TISSUE=Brain;  
 RX MEDLINE=89346754; PubMed=2569763;  
 RA de Sauvage F., Octave J.N.;  
 RT "A novel mRNA of the A4 amyloid precursor gene coding for a possibly  
 RT secreted protein.";  
 RL Science 245:651-653(1989).  
 RN [15]  
 RP PARTIAL SEQUENCE FROM N.A. (ISOFORM APP695).  
 RC TISSUE=Brain;  
 RX MEDLINE=87231971; PubMed=3035574;  
 RA Robakis N.K., Ramakrishna N., Wolfe G., Wisniewski H.M.;  
 RT "Molecular cloning and characterization of a cDNA encoding the  
 RT cerebrovascular and the neuritic plaque amyloid peptides.";  
 RL Proc. Natl. Acad. Sci. U.S.A. 84:4190-4194(1987).  
 RN [16]  
 RP SEQUENCE OF 286-366 FROM N.A.  
 RX MEDLINE=88122640; PubMed=2893290;  
 RA Tanzi R.E., McClatchey A.I., Lamperti E.D., Villa-Komaroff L.,  
 RA Gusella J.F., Neve R.L.;  
 RT "Protease inhibitor domain encoded by an amyloid protein precursor  
 RT mRNA associated with Alzheimer's disease.";  
 RL Nature 331:528-530(1988).  
 RN [17]  
 RP SEQUENCE OF 287-367 FROM N.A.  
 RX MEDLINE=88122641; PubMed=2893291;  
 RA Kitaguchi N., Takahashi Y., Tokushima Y., Shiojiri S., Ito H.;  
 RT "Novel precursor of Alzheimer's disease amyloid protein shows  
 RT protease inhibitory activity.";  
 RL Nature 331:530-532(1988).  
 RN [18]  
 RP SEQUENCE OF 507-770 FROM N.A.  
 RC TISSUE=Brain cortex;  
 RX MEDLINE=88124954; PubMed=2893379;  
 RA Zain S.B., Salim M., Chou W.G., Sajdel-Sulkowska E.M., Majocha R.E.,  
 RA Marotta C.A.;  
 RT "Molecular cloning of amyloid cDNA derived from mRNA of the Alzheimer  
 RT disease brain: coding and noncoding regions of the fetal precursor  
 RT mRNA are expressed in the cortex.";  
 RL Proc. Natl. Acad. Sci. U.S.A. 85:929-933(1988).  
 RN [19]  
 RP SEQUENCE OF 523-555, AND COLLAGEN-BINDING DOMAIN.  
 RX MEDLINE=96139497; PubMed=8576160;  
 RA Behr D., Hesse L., Masters C.L., Multhaup G.;  
 RT "Regulation of amyloid protein precursor (APP) binding to collagen and  
 RT mapping of the binding sites on APP and collagen type I.";  
 RL J. Biol. Chem. 271:1613-1620(1996).  
 RN [20]  
 RP SEQUENCE OF 655-737 FROM N.A., AND VARIANTS AD PHE-717; AD ILE-717  
 RP AND AD GLY-717.  
 RX MEDLINE=93236601; PubMed=8476439;  
 RA Denman R.B., Rosenzwaig R., Miller D.L.;  
 RT "A system for studying the effect(s) of familial Alzheimer disease  
 RT mutations on the processing of the beta-amyloid peptide precursor.";  
 RL Biochem. Biophys. Res. Commun. 192:96-103(1993).  
 RN [21]  
 RP SEQUENCE OF 656-737 FROM N.A.



RX MEDLINE=89392030; PubMed=2675837;  
RA Johnstone E.M., Chaney M.O., Moore R.E., Ward K.E., Norris F.H.,  
RA Little S.P.;  
RT "Alzheimer's disease amyloid peptide is encoded by two exons and shows  
RT similarity to soybean trypsin inhibitor.";  
RL Biochem. Biophys. Res. Commun. 163:1248-1255(1989).  
RN [22]

Query Match 98.1%; Score 3582.5; DB 1; Length 770;  
Best Local Similarity 89.9%; Pred. No. 1.8e-168;  
Matches 692; Conservative 2; Mismatches 1; Indels 75; Gaps 1;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE	240
Qy	241	EADDDDEDGDEVEEEAEPEYEEATERTTTSIATTTTTTTESVEEVVR-----	288
Db	241	EADDDDEDGDEVEEEAEPEYEEATERTTTSIATTTTTTTESVEEVVREVCSEQAETGPC	300
Qy	289	-----	288
Db	301	RAMISRWFVDVTEGKCAPFFYGGCGGNRNNFDTEEYCMVCGSAMSQSLLKTTQEPLARD	360
Qy	289	---VPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQA	345
		:	
Db	361	PVKLPPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQA	420
Qy	346	KNLPKADKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITAL	405
Db	421	KNLPKADKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITAL	480
Qy	406	QAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYER	465
Db	481	QAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYER	540
Qy	466	MNQSLSLLYNVPAAVAEEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDALMPSLTET	525
Db	541	MNQSLSLLYNVPAAVAEEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDALMPSLTET	600
Qy	526	KTTVELLPVNGEFSLDDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTN	585
Db	601	KTTVELLPVNGEFSLDDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTN	660
Qy	586	IKTEEISEVNLDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITL	645

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Db      661 IKTEEISEVKMDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIAITVIVITL 720
Qy      646 VMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695
Db      721 VMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 770

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## RESULT 2

### A4\_MACFA

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ID      A4_MACFA          STANDARD;          PRT;    770 AA.
AC      P53601; Q95KN7;
DT      01-OCT-1996 (Rel. 34, Created)
DT      28-FEB-2003 (Rel. 41, Last sequence update)
DT      28-FEB-2003 (Rel. 41, Last annotation update)
DE      Amyloid beta A4 protein precursor (APP) (ABPP) (Alzheimer's disease
DE      amyloid protein homolog) [Contains: Soluble APP-alpha (S-APP-alpha);
DE      Soluble APP-beta (S-APP-beta); C99; Beta-amyloid protein 42 (Beta-
DE      APP42); Beta-amyloid protein 40 (Beta-APP40); C83; P3(42); P3(40);
DE      Gamma-CTF(59) (Gamma-secretase C-terminal fragment 59); Gamma-CTF(57)
DE      (Gamma-secretase C-terminal fragment 57); Gamma-CTF(50) (Gamma-
DE      secretase C-terminal fragment 50); C31].
GN      APP.
OS      Macaca fascicularis (Crab eating macaque) (Cynomolgus monkey).
OC      Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC      Mammalia; Eutheria; Primates; Catarrhini; Cercopithecidae;
OC      Cercopithecinae; Macaca.
OX      NCBI_TaxID=9541;
RN      [1]
RP      SEQUENCE FROM N.A. (ISOFORMS APP695 AND APP770).
RC      TISSUE=Cerebellum;
RX      MEDLINE=91273117; PubMed=1905108;
RA      Podlisny M.B., Tolan D.R., Selkoe D.J.;
RT      "Homology of the amyloid beta protein precursor in monkey and human
RT      supports a primate model for beta amyloidosis in Alzheimer's
RT      disease.";
RL      Am. J. Pathol. 138:1423-1435(1991).
CC      -!- FUNCTION: Functions as a cell surface receptor and performs
CC      physiological functions on the surface of neurons relevant to
CC      neurite growth, neuronal adhesion and axonogenesis. Involved in
CC      cell mobility and transcription regulation through protein-protein
CC      interactions (By similarity). Can promote transcription activation
CC      through binding to APBB1/Tip60 and inhibit Notch signaling through
CC      interaction with Numb (By similarity). Couples to apoptosis-
CC      inducing pathways such as those mediated by G(O) and JIP (By
CC      similarity). Inhibits G(O) alpha ATPase activity (By similarity).
CC      Acts as a kinesin I membrane receptor, mediating the axonal
CC      transport of beta-secretase and presenilin 1 (By similarity). May
CC      be involved in copper homeostasis/oxidative stress through copper
CC      ion reduction. In vitro, copper-metallated APP induces neuronal
CC      death directly or is potentiated through Cu(II)-mediated low-
CC      density lipoprotein oxidation (By similarity). Can regulate
CC      neurite outgrowth through binding to components of the
CC      extracellular matrix such as heparin and collagen I and IV (By
CC      similarity). The splice isoforms that contain the BPTI domain
CC      possess protease inhibitor activity (By similarity).
CC      -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators

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CC with metal-reducing activity. Bind transient metals such as  
 CC copper, zinc and iron (By similarity).

CC -!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved  
 CC peptides, including C31, are potent enhancers of neuronal  
 CC apoptosis (By similarity).

CC -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several  
 CC cytoplasmic proteins, including APBB family members, the APBA  
 CC family, MAPK8IP1, and SHC1, Numb and Dab1 (By similarity). Binding  
 CC to Dab1 inhibits its serine phosphorylation (By similarity). Also  
 CC interacts with GPCR-like protein BPP, FPRL1, APPBP1, IB1, KNS2  
 CC (via its TPR domains) (By similarity), APPBP2 (via BaSS) and DDB1.  
 CC In vitro, it binds MAPT via the MT-binding domains (By  
 CC similarity). Associates with microtubules in the presence of ATP  
 CC and in a kinesin-dependent manner (By similarity).

CC -!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface  
 CC protein that rapidly becomes internalized via clathrin-coated  
 CC pits. During maturation, the immature APP (N-glycosylated in the  
 CC endoplasmic reticulum) moves to the Golgi complex where complete  
 CC maturation occurs (O-glycosylated and sulfated). After alpha-  
 CC secretase cleavage, soluble APP is released into the extracellular  
 CC space and the C-terminal is internalized to endosomes and  
 CC lysosomes. Some APP accumulates in secretory transport vesicles  
 CC leaving the late Golgi compartment and returns to the cell  
 CC surface. Gamma-CTF(59) peptide is located to both the cytoplasm  
 CC and nuclei of neurons (By similarity).

CC -!- ALTERNATIVE PRODUCTS:  
 CC Event=Alternative splicing; Named isoforms=2;  
 CC Comment=Additional isoforms seem to exist;  
 CC Name=APP770;  
 CC IsoId=P53601-1; Sequence=Displayed;  
 CC Name=APP695;  
 CC IsoId=P53601-2; Sequence=VSP\_000010, VSP\_000011;

CC -!- DOMAIN: The basolateral sorting signal (BaSS) is required for  
 CC sorting of membrane proteins to the basolateral surface of  
 CC epithelial cells (By similarity).

CC -!- DOMAIN: The NPXY sequence motif found in many tyrosine-  
 CC phosphorylated proteins is required for the specific binding of  
 CC the PID domain. However additional amino acids either N- or C-  
 CC terminal to the NPXY motif are often required for complete  
 CC interaction. The PID domain-containing proteins which bind APP  
 CC require the YENPTY motif for full interaction. These interactions  
 CC are independent of phosphorylation on the terminal tyrosine  
 CC residue. The NPXY site is also involved in clathrin-mediated  
 CC endocytosis (By similarity).

CC -!- PTM: Proteolytically processed under normal cellular conditions.  
 CC Cleavage by alpha-secretase or alternatively by beta-secretase  
 CC leads to generation and extracellular release of soluble APP  
 CC peptides, S-APP-alpha and S-APP-beta, respectively, and the  
 CC retention of corresponding membrane-anchored C-terminal fragments,  
 CC C83 and C99. Subsequent processing of C83 by gamma-secretase  
 CC yields P3 peptides. This is the major secretory pathway and is  
 CC nonamyloidogenic. Alternatively, presenilin/nicastrin-mediated  
 CC gamma-secretase processing of C99 releases the amyloid beta  
 CC proteins, amyloid-beta 40 (Abeta40) and amyloid-beta 42 (Abeta42),  
 CC major components of amyloid plaques, and the cytotoxic C-terminal  
 CC fragments, gamma-CTF(50), gamma-CTF(57) and gamma-CTF(59) (By  
 CC similarity).

CC -!- PTM: Proteolytically cleaved by caspases during neuronal apoptosis  
 CC (By similarity). Cleavage at Asp-739 by either caspase-3, -8 or -9  
 CC results in the production of the neurotoxic C31 peptide and the  
 CC increased production of beta-amyloid peptides (By similarity).  
 CC -!- PTM: N- and O-glycosylated (By similarity).  
 CC -!- PTM: Phosphorylation in the C-terminal on tyrosine, threonine and  
 CC serine residues is neuron-specific. Phosphorylation can affect APP  
 CC processing, neuronal differentiation and interaction with other  
 CC proteins (By similarity).  
 CC -!- MISCELLANEOUS: Chelation of metal ions, notably copper, iron and  
 CC zinc, can induce histidine-bridging between beta-amyloid molecules  
 CC resulting in beta-amyloid-metal aggregates (By similarity).  
 CC Extracellular zinc-binding increases binding of heparin to APP and  
 CC inhibits collagen-binding (By similarity).  
 CC -!- SIMILARITY: Belongs to the APP family.  
 CC -!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.

CC -----  
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DR EMBL; M58727; AAA36829.1; -.  
 DR EMBL; M58726; AAA36828.1; -.  
 DR HSSP; P05067; 1AAP.  
 DR InterPro; IPR008155; A4\_APP.  
 DR InterPro; IPR008154; A4\_extra.  
 DR InterPro; IPR001255; Beta-APP.  
 DR InterPro; IPR002223; Kunitz\_BPTI.  
 DR Pfam; PF02177; A4\_EXTRA; 1.  
 DR Pfam; PF03494; Beta-APP; 1.  
 DR Pfam; PF00014; Kunitz\_BPTI; 1.  
 DR PRINTS; PR00203; AMYLOIDA4.  
 DR PRINTS; PR00759; BASICPTASE.  
 DR ProDom; PD000222; Kunitz\_BPTI; 1.  
 DR SMART; SM00006; A4\_EXTRA; 1.  
 DR SMART; SM00131; KU; 1.  
 DR PROSITE; PS00319; A4\_EXTRA; 1.  
 DR PROSITE; PS00320; A4\_INTRA; 1.  
 DR PROSITE; PS00280; BPTI\_KUNITZ\_1; 1.  
 DR PROSITE; PS50279; BPTI\_KUNITZ\_2; 1.  
 KW Apoptosis; Endocytosis; Cell adhesion; Serine protease inhibitor;  
 KW Coated pits; Neurone; Heparin-binding; Metal-binding; Copper; Iron;  
 KW Zinc; Signal; Transmembrane; Glycoprotein; Phosphorylation;  
 KW Proteoglycan; Alternative splicing; Amyloid.  
 FT SIGNAL 1 17 BY SIMILARITY.  
 FT CHAIN 18 770 AMYLOID BETA A4 PROTEIN.  
 FT CHAIN 18 687 SOLUBLE APP-ALPHA (POTENTIAL).  
 FT CHAIN 18 671 SOLUBLE APP-BETA (POTENTIAL).  
 FT CHAIN 672 770 C99 (POTENTIAL).  
 FT CHAIN 672 713 BETA-AMYLOID PROTEIN 42 (POTENTIAL).  
 FT CHAIN 672 711 BETA-AMYLOID PROTEIN 40 (POTENTIAL).  
 FT CHAIN 688 770 C83 (POTENTIAL).  
 FT CHAIN 688 713 P3(42) (POTENTIAL).

FT	CHAIN	688	711	P3(40) (POTENTIAL).
FT	CHAIN	712	770	GAMMA-CTF(59) (POTENTIAL).
FT	CHAIN	714	770	GAMMA-CTF(57) (POTENTIAL).
FT	CHAIN	721	770	GAMMA-CTF(50) (POTENTIAL).
FT	CHAIN	740	770	C31 (POTENTIAL).
FT	DOMAIN	18	699	EXTRACELLULAR (POTENTIAL).
FT	TRANSMEM	700	723	POTENTIAL.
FT	DOMAIN	724	770	CYTOPLASMIC (POTENTIAL).
FT	DOMAIN	96	110	HEPARIN-BINDING (BY SIMILARITY).
FT	DOMAIN	181	188	ZINC-BINDING (BY SIMILARITY).
FT	DOMAIN	291	341	BPTI/KUNITZ INHIBITOR.
FT	DOMAIN	391	423	HEPARIN-BINDING (BY SIMILARITY).
FT	DOMAIN	491	522	HEPARIN-BINDING (BY SIMILARITY).
FT	DOMAIN	523	540	COLLAGEN-BINDING (BY SIMILARITY).
FT	DOMAIN	732	751	INTERACTION WITH G(O)-ALPHA
FT				(BY SIMILARITY).
FT	DOMAIN	230	260	ASP/GLU-RICH (ACIDIC).
FT	DOMAIN	274	280	POLY-THR.
FT	SITE	144	144	REQUIRED FOR COPPER(II) REDUCTION
FT				(BY SIMILARITY).
FT	ACT_SITE	301	302	REACTIVE BOND (BY SIMILARITY).
FT	SITE	671	672	CLEAVAGE (BY BETA-SECRETASE)
FT				(BY SIMILARITY).
FT	SITE	672	673	CLEAVAGE (BY CASPASE-6) (BY SIMILARITY).
FT	SITE	687	688	CLEAVAGE (BY ALPHA-SECRETASE)
FT				(BY SIMILARITY).
FT	SITE	704	704	IMPLICATED IN FREE RADICAL PROPAGATION
FT				(BY SIMILARITY).
FT	SITE	706	706	INVOLVED IN OXIDATIVE REACTIONS
FT				(BY SIMILARITY).
FT	SITE	711	712	CLEAVAGE (BY GAMMA-SECRETASE; SITE 1)
FT				(BY SIMILARITY).
FT	SITE	713	714	CLEAVAGE (BY GAMMA-SECRETASE; SITE 2)
FT				(BY SIMILARITY).
FT	SITE	720	721	CLEAVAGE (BY GAMMA-SECRETASE; SITE 3)
FT				(BY SIMILARITY).
FT	SITE	724	734	BASOLATERAL SORTING SIGNAL
FT				(BY SIMILARITY).
FT	SITE	739	740	CLEAVAGE (BY CASPASES-3,-6,-8 OR -9)

Query Match 98.1%; Score 3582.5; DB 1; Length 770;  
 Best Local Similarity 89.9%; Pred. No. 1.8e-168;  
 Matches 692; Conservative 2; Mismatches 1; Indels 75; Gaps 1;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHNMNVQNGKWDSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHNMNVQNGKWDSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240

Db	181	 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVR-----	288
Db	241	 EADDDDEDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVREVCSEAETGPC	300
Qy	289	-----	288
Db	301	RAMISRWFVDVTEGKCAPFFYGGCGGNRNNFDTEEYCMVCGSVMSQSLRKTTREPLTRD	360
Qy	289	---VPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQA	345
Db	361	:      PVKLPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQA	420
Qy	346	KNLPKADKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITAL	405
Db	421	 KNLPKADKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITAL	480
Qy	406	QAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYER	465
Db	481	 QAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYER	540
Qy	466	MNQSLSLLYNVPAAVEEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDALMPSLTET	525
Db	541	 MNQSLSLLYNVPAAVEEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDALMPSLTET	600
Qy	526	KTTVELLPVNGEFSLDDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTN	585
Db	601	 KTTVELLPVNGEFSLDDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTN	660
Qy	586	IKTEEISEVNLDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITL	645
Db	661	:      IKTEEISEVKMDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITL	720
Qy	646	VMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN	695
Db	721	 VMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN	770

# RESULT 3

## A4\_SAISC

ID A4\_SAISC STANDARD; PRT; 751 AA.  
AC Q95241;  
DT 15-DEC-1998 (Rel. 37, Created)  
DT 15-DEC-1998 (Rel. 37, Last sequence update)  
DT 10-OCT-2003 (Rel. 42, Last annotation update)  
DE Amyloid beta A4 protein precursor (APP) (Alzheimer's disease amyloid  
DE protein homolog) [Contains: Soluble APP-alpha (S-APP-alpha); Soluble  
DE APP-beta (S-APP-beta); C99; Beta-amyloid protein 42 (Beta-APP42);  
DE Beta-amyloid protein 40 (Beta-APP40); C83; P3(42); P3(40); Gamma-  
DE CTF(59) (Gamma-secretase C-terminal fragment 59); Gamma-CTF(57)  
DE (Gamma-secretase C-terminal fragment 57); Gamma-CTF(50) (Gamma-  
DE secretase C-terminal fragment 50); C31].  
GN APP.  
OS Saimiri sciureus (Common squirrel monkey).  
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;

OC Mammalia; Eutheria; Primates; Platyrrhini; Cebidae; Cebinae; Saimiri.  
 OX NCBI\_TaxID=9521;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RC TISSUE=Kidney, and Liver;  
 RX MEDLINE=96108492; PubMed=8532114;  
 RA Levy E., Amorim A., Frangione B., Walker L.C.;  
 RT "Beta-amyloid precursor protein gene in squirrel monkeys with  
 RT cerebral amyloid angiopathy.";  
 RL Neurobiol. Aging 16:805-808(1995).  
 CC -!- FUNCTION: Functions as a cell surface receptor and performs  
 CC physiological functions on the surface of neurons relevant to  
 CC neurite growth, neuronal adhesion and axonogenesis. Involved in  
 CC cell mobility and transcription regulation through protein-protein  
 CC interactions (By similarity). Can promote transcription activation  
 CC through binding to APBB1/Tip60 and inhibit Notch signaling through  
 CC interaction with Numb (By similarity). Couples to apoptosis-  
 CC inducing pathways such as those mediated by G(O) and JIP (By  
 CC similarity). Inhibits G(O) alpha ATPase activity (By similarity).  
 CC Acts as a kinesin I membrane receptor, mediating the axonal  
 CC transport of beta-secretase and presenilin 1 (By similarity). May  
 CC be involved in copper homeostasis/oxidative stress through copper  
 CC ion reduction. In vitro, copper-metallated APP induces neuronal  
 CC death directly or is potentiated through Cu(II)-mediated low-  
 CC density lipoprotein oxidation (By similarity). Can regulate  
 CC neurite outgrowth through binding to components of the  
 CC extracellular matrix such as heparin and collagen I and IV (By  
 CC similarity). The splice isoforms that contain the BPTI domain  
 CC possess protease inhibitor activity (By similarity).  
 CC -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators  
 CC with metal-reducing activity. Bind transient metals such as  
 CC copper, zinc and iron (By similarity).  
 CC -!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved  
 CC peptides, including C31, are potent enhancers of neuronal  
 CC apoptosis (By similarity).  
 CC -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several  
 CC cytoplasmic proteins, including APBB family members, the APBA  
 CC family, MAPK8IP1, and SHC1, Numb and Dab1 (By similarity). Binding  
 CC to Dab1 inhibits its serine phosphorylation (By similarity). Also  
 CC interacts with GPCR-like protein BPP, FPRL1, APPBP1, IB1, KNS2  
 CC (via its TPR domains) (By similarity), APPBP2 (via BaSS) and DDB1.  
 CC In vitro, it binds MAPT via the MT-binding domains (By  
 CC similarity). Associates with microtubules in the presence of ATP  
 CC and in a kinesin-dependent manner (By similarity).  
 CC -!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface  
 CC protein that rapidly becomes internalized via clathrin-coated  
 CC pits. During maturation, the immature APP (N-glycosylated in the  
 CC endoplasmic reticulum) moves to the Golgi complex where complete  
 CC maturation occurs (O-glycosylated and sulfated). After alpha-  
 CC secretase cleavage, soluble APP is released into the extracellular  
 CC space and the C-terminal is internalized to endosomes and  
 CC lysosomes. Some APP accumulates in secretory transport vesicles  
 CC leaving the late Golgi compartment and returns to the cell  
 CC surface. Gamma-CTF(59) peptide is located to both the cytoplasm  
 CC and nuclei of neurons (By similarity).  
 CC -!- ALTERNATIVE PRODUCTS:  
 CC Event=Alternative splicing; Named isoforms=2;

CC           Comment=Additional isoforms seem to exist;  
 CC           Name=APP770;  
 CC           IsoId=Q95241-1; Sequence=Displayed;  
 CC           Name=APP695;  
 CC           IsoId=Q95241-2; Sequence=Not described;  
 CC    -!- DOMAIN: The basolateral sorting signal (BaSS) is required for  
 CC           sorting of membrane proteins to the basolateral surface of  
 CC           epithelial cells (By similarity).  
 CC    -!- DOMAIN: The NPXY sequence motif found in many tyrosine-  
 CC           phosphorylated proteins is required for the specific binding of  
 CC           the PID domain. However additional amino acids either N- or C-  
 CC           terminal to the NPXY motif are often required for complete  
 CC           interaction. The PID domain-containing proteins which bind APP  
 CC           require the YENPTY motif for full interaction. These interactions  
 CC           are independent of phosphorylation on the terminal tyrosine  
 CC           residue. The NPXY site is also involved in clathrin-mediated  
 CC           endocytosis (By similarity).  
 CC    -!- PTM: Proteolytically processed under normal cellular conditions.  
 CC           Cleavage by alpha-secretase or alternatively by beta-secretase  
 CC           leads to generation and extracellular release of soluble APP  
 CC           peptides, S-APP-alpha and S-APP-beta, respectively, and the  
 CC           retention of corresponding membrane-anchored C-terminal fragments,  
 CC           C83 and C99. Subsequent processing of C83 by gamma-secretase  
 CC           yields P3 peptides. This is the major secretory pathway and is  
 CC           nonamyloidogenic. Alternatively, presenilin/nicastrin-mediated  
 CC           gamma-secretase processing of C99 releases the amyloid beta  
 CC           proteins, amyloid-beta 40 (Abeta40) and amyloid-beta 42 (Abeta42),  
 CC           major components of amyloid plaques, and the cytotoxic C-terminal  
 CC           fragments, gamma-CTF(50), gamma-CTF(57) and gamma-CTF(59) (By  
 CC           similarity).  
 CC    -!- PTM: Proteolytically cleaved by caspases during neuronal apoptosis.  
 CC           (By similarity). Cleavage at Asp-720 by either caspase-3, -8 or -9  
 CC           results in the production of the neurotoxic C31 peptide and the  
 CC           increased production of beta-amyloid peptides (By similarity).  
 CC    -!- PTM: N- and O-glycosylated (By similarity).  
 CC    -!- PTM: Phosphorylation in the C-terminal on tyrosine, threonine and  
 CC           serine residues is neuron-specific. Phosphorylation can affect APP  
 CC           processing, neuronal differentiation and interaction with other  
 CC           proteins (By similarity).  
 CC    -!- MISCELLANEOUS: Chelation of metal ions, notably copper, iron and  
 CC           zinc, can induce histidine-bridging between beta-amyloid molecules  
 CC           resulting in beta-amyloid-metal aggregates (By similarity).  
 CC           Extracellular zinc-binding increases binding of heparin to APP and  
 CC           inhibits collagen-binding (By similarity).  
 CC    -!- SIMILARITY: Belongs to the APP family.  
 CC    -!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.  
 CC    -----  
 CC    This SWISS-PROT entry is copyright. It is produced through a collaboration  
 CC    between the Swiss Institute of Bioinformatics and the EMBL outstation -  
 CC    the European Bioinformatics Institute. There are no restrictions on its  
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 CC    or send an email to [license@isb-sib.ch](mailto:license@isb-sib.ch)).  
 CC    -----  
 DR    EMBL; S81024; AAD14347.1; -.  
 DR    HSSP; P05067; 1AAP.



DR InterPro; IPR008155; A4\_APP.  
 DR InterPro; IPR008154; A4\_extra.  
 DR InterPro; IPR001255; Beta-APP.  
 DR InterPro; IPR002223; Kunitz\_BPTI.  
 DR Pfam; PF02177; A4\_EXTRA; 1.  
 DR Pfam; PF03494; Beta-APP; 1.  
 DR Pfam; PF00014; Kunitz\_BPTI; 1.  
 DR PRINTS; PR00203; AMYLOIDA4.  
 DR PRINTS; PR00759; BASICPTASE.  
 DR ProDom; PD000222; Kunitz\_BPTI; 1.  
 DR SMART; SM00006; A4\_EXTRA; 1.  
 DR SMART; SM00131; KU; 1.  
 DR PROSITE; PS00319; A4\_EXTRA; 1.  
 DR PROSITE; PS00320; A4\_INTRA; 1.  
 DR PROSITE; PS00280; BPTI\_KUNITZ\_1; 1.  
 DR PROSITE; PS50279; BPTI\_KUNITZ\_2; 1.  
 KW Apoptosis; Endocytosis; Cell adhesion; Serine protease inhibitor;  
 KW Coated pits; Neurone; Heparin-binding; Metal-binding; Copper; Iron;  
 KW Zinc; Signal; Transmembrane; Glycoprotein; Phosphorylation;  
 KW Proteoglycan; Amyloid; Alternative splicing.  
 FT SIGNAL 1 17 BY SIMILARITY.  
 FT CHAIN 18 751 A4 PROTEIN.  
 FT CHAIN 18 668 SOLUBLE APP-ALPHA (POTENTIAL).  
 FT CHAIN 18 652 SOLUBLE APP-BETA (POTENTIAL).  
 FT CHAIN 653 751 C99 (POTENTIAL).  
 FT CHAIN 653 694 BETA-AMYLOID PROTEIN 42 (POTENTIAL).  
 FT CHAIN 653 692 BETA-AMYLOID PROTEIN 40 (POTENTIAL).  
 FT CHAIN 669 751 C83 (POTENTIAL).  
 FT CHAIN 669 694 P3(42) (POTENTIAL).  
 FT CHAIN 669 692 P3(40) (POTENTIAL).  
 FT CHAIN 693 751 GAMMA-CTF(59) (POTENTIAL).  
 FT CHAIN 695 751 GAMMA-CTF(57) (POTENTIAL).  
 FT CHAIN 702 751 GAMMA-CTF(50) (POTENTIAL).  
 FT CHAIN 721 751 C31 (POTENTIAL).  
 FT DOMAIN 18 680 EXTRACELLULAR (POTENTIAL).  
 FT TRANSMEM 681 704 POTENTIAL.  
 FT DOMAIN 705 751 CYTOPLASMIC (POTENTIAL).  
 FT DOMAIN 96 110 HEPARIN-BINDING (BY SIMILARITY).  
 FT DOMAIN 181 188 ZINC-BINDING (BY SIMILARITY).  
 FT DOMAIN 291 341 BPTI/KUNITZ INHIBITOR.  
 FT DOMAIN 316 344 HEPARIN-BINDING (BY SIMILARITY).  
 FT DOMAIN 363 428 HEPARIN-BINDING (BY SIMILARITY).  
 FT DOMAIN 504 521 COLLAGEN-BINDING (BY SIMILARITY).  
 FT DOMAIN 713 732 INTERACTION WITH G(O)-ALPHA  
 FT (BY SIMILARITY).  
 FT DOMAIN 230 260 ASP/GLU-RICH (ACIDIC).  
 FT DOMAIN 274 280 POLY-THR.  
 FT SITE 144 144 REQUIRED FOR COPPER(II) REDUCTION  
 FT (BY SIMILARITY).  
 FT ACT\_SITE 301 302 REACTIVE BOND.  
 FT SITE 652 653 CLEAVAGE (BY BETA-SECRETASE)  
 FT (BY SIMILARITY).  
 FT SITE 653 654 CLEAVAGE (BY CASPASE-6) (BY SIMILARITY).  
 FT SITE 668 669 CLEAVAGE (BY ALPHA-SECRETASE)  
 FT (BY SIMILARITY).  
 FT SITE 685 685 INVOLVED IN FREE RADICAL PROPAGATION  
 FT (BY SIMILARITY).

FT	SITE	687	687	INVOLVED IN OXIDATIVE REACTIONS
FT				(BY SIMILARITY).
FT	SITE	692	693	CLEAVAGE (BY GAMMA-SECRETASE; SITE 1)
FT				(BY SIMILARITY).
FT	SITE	694	695	CLEAVAGE (BY GAMMA-SECRETASE; SITE 2)
FT				(BY SIMILARITY).
FT	SITE	701	702	CLEAVAGE (BY GAMMA-SECRETASE; SITE 3)
FT				(BY SIMILARITY).
FT	SITE	705	715	BASOLATERAL SORTING SIGNAL
FT				(BY SIMILARITY).
FT	SITE	720	721	CLEAVAGE (BY CASPASES-3,-6,-8 OR -9)
FT				(BY SIMILARITY).
FT	SITE	738	741	ENDOCYTOSIS SIGNAL.
FT	SITE	740	743	NPXY MOTIF.

Query Match 97.9%; Score 3576; DB 1; Length 751;  
 Best Local Similarity 91.7%; Pred. No. 3.6e-168;  
 Matches 689; Conservative 3; Mismatches 3; Indels 56; Gaps 1;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRDRKQCKTHPHIVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE	240
		:	
Db	181	GVEFVCCPLAEESDHVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE	240
Qy	241	EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVR-----	288
Db	241	EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVREVCSEAETGPC	300
Qy	289	-----VPTTAASTPDAVDKYL	304
		:	
Db	301	RAMISRWFVDVTEGKCAPFFYGGCGGNRNNFDTEEYCMVCGSVIPTTAASTPDAVDKYL	360
Qy	305	ETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHFQEKV	364
Db	361	ETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHFQEKV	420
Qy	365	ESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLKKYVR	424
Db	421	ESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLKKYVR	480
Qy	425	AEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVAEEIQ	484
Db	481	AEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVAEEIQ	540
Qy	485	DEVDELLQKEQNYSDVLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSLDDLQ	544

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Db      541 DEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSLLDLQ 600
Qy      545 PWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEI SEVNLD AEF RHDS 604
      |||
Db      601 PWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEI SEVKMD AEF RHDS 660
Qy      605 GYEVHHQKL VFFAEDVGSNKGAI IGLMVGGVVIATVIVITLVMLKKKQYTSI HHGVVEVD 664
      |||
Db      661 GYEVHHQKL VFFAEDVGSNKGAI IGLMVGGVVIATVIVITLVMLKKKQYTSI HHGVVEVD 720
Qy      665 AAVTPEERHLSKMQQNGYENPTYKFFE QMQN 695
      |||
Db      721 AAVTPEERHLSKMQQNGYENPTYKFFE QMQN 751

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#### RESULT 4

##### A4\_PIG

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ID      A4_PIG          STANDARD;          PRT;    770 AA.
AC      P79307; Q29023; Q9TUI0;
DT      01-NOV-1997 (Rel. 35, Created)
DT      10-OCT-2003 (Rel. 42, Last sequence update)
DT      10-OCT-2003 (Rel. 42, Last annotation update)
DE      Amyloid beta A4 protein precursor (APP) (ABPP) (Alzheimer's disease
DE      amyloid protein homolog) [Contains: Soluble APP-alpha (S-APP-alpha);
DE      Soluble APP-beta (S-APP-beta); C99; Beta-amyloid protein 42 (Beta-
DE      APP42); Beta-amyloid protein 40 (Beta-APP40); C83; P3(42); P3(40);
DE      Gamma-CTF(59) (Gamma-secretase C-terminal fragment 59); Gamma-CTF(57)
DE      (Gamma-secretase C-terminal fragment 57); Gamma-CTF(50) (Gamma-
DE      secretase C-terminal fragment 50); C31].
OS      Sus scrofa (Pig).
OC      Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC      Mammalia; Eutheria; Cetartiodactyla; Suina; Suidae; Sus.
OX      NCBI_TaxID=9823;
RN      [1]
RP      SEQUENCE FROM N.A.
RA      Kimura A., Takahashi T.;
RT      "Amyloid precursor protein 770.";
RL      Submitted (SEP-1999) to the EMBL/GenBank/DDBJ databases.
RN      [2]
RP      SEQUENCE OF 1-136 FROM N.A.
RC      TISSUE=Small intestine;
RA      Winteroe A.K., Fredholm M.;
RT      "Evaluation and characterization of a porcine small intestine cDNA
RT      library.";
RL      Submitted (JAN-1997) to the EMBL/GenBank/DDBJ databases.
RN      [3]
RP      SEQUENCE OF 667-723 FROM N.A.
RC      TISSUE=Brain;
RX      MEDLINE=92017079; PubMed=1656157;
RA      Johnstone E.M., Chaney M.O., Norris F.H., Pascual R., Little S.P.;
RT      "Conservation of the sequence of the Alzheimer's disease amyloid
RT      peptide in dog, polar bear and five other mammals by cross-species
RT      polymerase chain reaction analysis.";
RL      Brain Res. Mol. Brain Res. 10:299-305(1991).
CC      -!- FUNCTION: Functions as a cell surface receptor and performs
CC      physiological functions on the surface of neurons relevant to
CC      neurite growth, neuronal adhesion and axonogenesis. Involved in

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cell mobility and transcription regulation through protein-protein interactions (By similarity). Can promote transcription activation through binding to APBB1/Tip60 and inhibit Notch signaling through interaction with Numb (By similarity). Couples to apoptosis-inducing pathways such as those mediated by G(O) and JIP (By similarity). Inhibits G(O) alpha ATPase activity (By similarity). Acts as a kinesin I membrane receptor, mediating the axonal transport of beta-secretase and presenilin 1 (By similarity). May be involved in copper homeostasis/oxidative stress through copper ion reduction (By similarity). In vitro, copper-metallated APP induces neuronal death directly or is potentiated through Cu(II)-mediated low-density lipoprotein oxidation (By similarity). Can regulate neurite outgrowth through binding to components of the extracellular matrix such as heparin and collagen I and IV (By similarity).

-!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators with metal-reducing activity. Bind transient metals such as copper, zinc and iron (By similarity).

-!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved peptides, including C31, are potent enhancers of neuronal apoptosis (By similarity).

-!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several cytoplasmic proteins, including APBB family members, the APBA family, MAPK8IP1, and SHC1, Numb and Dab1 (By similarity). Binding to Dab1 inhibits its serine phosphorylation (By similarity). Also interacts with GPCR-like protein BPP, FPRL1, APPBP1, IB1, KNS2 (via its TPR domains) (By similarity), APPBP2 (via BaSS) and DDB1. In vitro, it binds MAPT via the MT-binding domains (By similarity). Associates with microtubules in the presence of ATP and in a kinesin-dependent manner (By similarity).

-!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface protein that rapidly becomes internalized via clathrin-coated pits. During maturation, the immature APP (N-glycosylated in the endoplasmic reticulum) moves to the Golgi complex where complete maturation occurs (O-glycosylated and sulfated). After alpha-secretase cleavage, soluble APP is released into the extracellular space and the C-terminal is internalized to endosomes and lysosomes. Some APP accumulates in secretory transport vesicles leaving the late Golgi compartment and returns to the cell surface. Gamma-CTF(59) peptide is located to both the cytoplasm and nuclei of neurons (By similarity).

-!- DOMAIN: The basolateral sorting signal (BaSS) is required for sorting of membrane proteins to the basolateral surface of epithelial cells (By similarity).

-!- DOMAIN: The NPXY sequence motif found in many tyrosine-phosphorylated proteins is required for the specific binding of the PID domain. However additional amino acids either N- or C-terminal to the NPXY motif are often required for complete interaction. The PID domain-containing proteins which bind APP require the YENPTY motif for full interaction. These interactions are independent of phosphorylation on the terminal tyrosine residue. The NPXY site is also involved in clathrin-mediated endocytosis (By similarity).

-!- PTM: Proteolytically processed under normal cellular conditions. Cleavage by alpha-secretase or alternatively by beta-secretase leads to generation and extracellular release of soluble APP peptides, S-APP-alpha and S-APP-beta, respectively, and the

CC retention of corresponding membrane-anchored C-terminal fragments,  
CC C83 and C99. Subsequent processing of C83 by gamma-secretase  
CC yields P3 peptides. This is the major secretory pathway and is  
CC nonamyloidogenic. Alternatively, presenilin/nicastrin-mediated  
CC gamma-secretase processing of C99 releases the amyloid beta  
CC proteins, amyloid-beta 40 (Abeta40) and amyloid-beta 42 (Abeta42),  
CC major components of amyloid plaques, and the cytotoxic C-terminal  
CC fragments, gamma-CTF(50), gamma-CTF(57) and gamma-CTF(59) (By  
CC similarity).

CC -!- PTM: Proteolytically cleaved by caspases during neuronal apoptosis  
CC (By similarity). Cleavage at Asp-739 by either caspase-3, -8 or -9  
CC results in the production of the neurotoxic C31 peptide and the  
CC increased production of beta-amyloid peptides (By similarity).

CC -!- PTM: N- and O-glycosylated (By similarity).

CC -!- PTM: Phosphorylation in the C-terminal on tyrosine, threonine and  
CC serine residues is neuron-specific. Phosphorylation can affect APP  
CC processing, neuronal differentiation and interaction with other  
CC proteins (By similarity).

CC -!- PTM: Extracellular binding and reduction of copper, results in a  
CC corresponding oxidation of Cys-144 and Cys-158, and the formation  
CC of a disulfide bond (By similarity).

CC -!- MISCELLANEOUS: Chelation of metal ions, notably copper, iron and  
CC zinc, can induce histidine-bridging between beta-amyloid molecules  
CC resulting in beta-amyloid-metal aggregates (By similarity).

CC Extracellular zinc-binding increases binding of heparin to APP and  
CC inhibits collagen-binding (By similarity).

CC -!- SIMILARITY: Belongs to the APP family.

CC -!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.

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CC -----

DR EMBL; AB032550; BAA84580.1; -.

DR EMBL; Z84022; CAB06313.1; -.

DR EMBL; X56127; CAA39592.1; -.

DR HSSP; P05067; 1AAP.

DR InterPro; IPR008155; A4\_APP.

DR InterPro; IPR008154; A4\_extra.

DR InterPro; IPR002223; Kunitz\_BPTI.

DR Pfam; PF02177; A4\_EXTRA; 1.

DR PRINTS; PR00203; AMYLOIDA4.

DR PRINTS; PR00759; BASICPTASE.

DR ProDom; PD000222; Kunitz\_BPTI; 1.

DR SMART; SM00006; A4\_EXTRA; 1.

DR SMART; SM00131; KU; 1.

DR PROSITE; PS00319; A4\_EXTRA; 1.

DR PROSITE; PS00320; A4\_INTRA; 1.

DR PROSITE; PS00280; BPTI\_KUNITZ\_1; 1.

DR PROSITE; PS50279; BPTI\_KUNITZ\_2; 1.

KW Apoptosis; Endocytosis; Cell adhesion; Serine protease inhibitor;

KW Coated pits; Neurone; Heparin-binding; Metal-binding; Copper; Iron;

KW Zinc; Signal; Transmembrane; Glycoprotein; Phosphorylation;



Db	61	TCIGTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRSRKQCKTHTHIVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
		:	
Db	181	GVEFVCCPLAEESDNIDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVADVEEE	240
Qy	241	EADDDDEDEDGDEVEEEAEEPYEEATERTTSIATTTTTTTSVEEVVR-----	288
		:	
Db	241	EAEDDEDEDGDEVEEEAEEPYEEATERTTSIATTTTTTTSVEEVVREVCSEQAETGPC	300
Qy	289	-----	288
Db	301	RAMISRWFYFDVTEGKCAPPFFYGGCGGNRNNFDTEEYCMVCGSVMSQSLLKTTQEHLPOD	360
Qy	289	---VPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQA	345
		:	
Db	361	PVKLPPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQA	420
Qy	346	KNLPKADKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITAL	405
Db	421	KNLPKADKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITAL	480
Qy	406	QAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYER	465
Db	481	QAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYER	540
Qy	466	MNQSLSLLYNVPAAVEEIQDEVDLLQKEQNYSDVLNMISEPRISYGNDALMPSLTET	525
Db	541	MNQSLSLLYNVPAAVEEIQDEVDLLQKEQNYSDVLNMISEPRISYGNDALMPSLTET	600
Qy	526	KTTVELLPVNGEFSLDDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTN	585
Db	601	KTTVELLPVNGEFSLDDLQPWHPFGVDSVPANTENEVEPVDARPAADRGLTTRPGSGLTN	660
Qy	586	IKTEEISEVNLDAEFRHDSGYEVHHQKLFFFAEDVGSNKGAIIGLMVGGVVIATVIVITL	645
		:	
Db	661	IKTEEISEVKMDAEFRHDSGYEVHHQKLFFFAEDVGSNKGAIIGLMVGGVVIATVIVITL	720
Qy	646	VMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQQMN	695
Db	721	VMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQQMN	770

RESULT 5

A4\_CAVPO

ID A4\_CAVPO STANDARD; PRT; 770 AA.

AC Q60495; Q60496;

DT 10-OCT-2003 (Rel. 42, Created)

DT 10-OCT-2003 (Rel. 42, Last sequence update)

DT 10-OCT-2003 (Rel. 42, Last annotation update)

DE Amyloid beta A4 protein precursor (APP) (ABPP) (Alzheimer's disease

DE amyloid protein homolog) [Contains: Soluble APP-alpha (S-APP-alpha);

DE Soluble APP-beta (S-APP-beta); CTF-alpha; CTF-beta; Beta-amyloid

DE protein 42 (Beta-APP42); Beta-amyloid protein 40 (Beta-APP40); P3(42);  
DE P3(40); CTF(59) (Gamma-secretase C-terminal fragment 59); Gamma-  
DE CTF(57) (Gamma-secretase C-terminal fragment 57); C31].  
GN APP.  
OS Cavia porcellus (Guinea pig).  
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
OC Mammalia; Eutheria; Rodentia; Hystricognathi; Caviidae; Cavia.  
OX NCBI\_TaxID=10141;  
RN [1]  
RP SEQUENCE FROM N.A., AND ALTERNATIVE SPLICING.  
RC TISSUE=Brain, and Liver;  
RX MEDLINE=97236426; PubMed=9116031;  
RA Beck M., Mueller D., Bigl V.;  
RT "Amyloid precursor protein in Guinea pigs - complete cDNA sequence and  
RT alternative splicing."  
RL Biochim. Biophys. Acta 1351:17-21(1997).  
RN [2]  
RP INTERACTION OF BETA-APP40 WITH APOE.  
RX MEDLINE=98007700; PubMed=9349544;  
RA Martel C.L., Mackic J.B., Matsubara E., Governale S., Miguel C.,  
RA Miao W., McComb J.G., Frangione B., Ghiso J., Zlokovic B.V.;  
RT "Isoform-specific effects of apolipoproteins E2, E3, and E4 on  
RT cerebral capillary sequestration and blood-brain barrier transport of  
RT circulating Alzheimer's amyloid beta."  
RL J. Neurochem. 69:1995-2004(1997).  
RN [3]  
RP PROCESSING.  
RX MEDLINE=20084499; PubMed=10619481;  
RA Beck M., Brueckner M.K., Holzer M., Kaap S., Pannicke T., Arendt T.,  
RA Bigl V.;  
RT "Guinea-pig primary cell cultures provide a model to study expression  
RT and amyloidogenic processing of endogenous amyloid precursor  
RT protein."  
RL Neuroscience 95:243-254(2000).  
RN [4]  
RP GAMMA-SECRETASE PROCESSING.  
RX MEDLINE=20576391; PubMed=11035007;  
RA Pinnix I., Musunuru U., Tun H., Sridharan A., Golde T., Eckman C.,  
RA Ziani-Cherif C., Onstead L., Sambamurti K.;  
RT "A novel gamma -secretase assay based on detection of the putative  
RT C-terminal fragment-gamma of amyloid beta protein precursor."  
RL J. Biol. Chem. 276:481-487(2001).  
CC -!- FUNCTION: Functions as a cell surface receptor and performs  
CC physiological functions on the surface of neurons relevant to  
CC neurite growth, neuronal adhesion and axonogenesis. Involved in  
CC cell mobility and transcription regulation through protein-protein  
CC interactions (By similarity). Can promote transcription activation  
CC through binding to APBB1/Tip60 and inhibit Notch signaling through  
CC interaction with Numb (By similarity). Couples to apoptosis-  
CC inducing pathways such as those mediated by G(O) and JIP (By  
CC similarity). Inhibits G(O) alpha ATPase activity (By similarity).  
CC Acts as a kinesin I membrane receptor, mediating the axonal  
CC transport of beta-secretase and presenilin 1 (By similarity). May  
CC be involved in copper homeostasis/oxidative stress through copper  
CC ion reduction (By similarity). In vitro, copper-metallated APP  
CC induces neuronal death directly or is potentiated through Cu(II)-  
CC mediated low-density lipoprotein oxidation (By similarity). Can



CC regulate neurite outgrowth through binding to components of the  
 CC extracellular matrix such as heparin and collagen I and IV (By  
 CC similarity). The splice isoforms that contain the BPTI domain  
 CC possess protease inhibitor activity (By similarity).  
 CC -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators  
 CC with metal-reducing activity. Bind transient metals such as  
 CC copper, zinc and iron. Beta-amyloid peptides bind to lipoproteins  
 CC and apolipoproteins E and J in the CSF and to HDL particles in  
 CC plasma, inhibiting metal-catalyzed oxidation of lipoproteins.  
 CC -!- FUNCTION: Appicans elicit adhesion of neural cells to the  
 CC extracellular matrix and may regulate neurite outgrowth in the  
 CC brain (By similarity).  
 CC -!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved  
 CC peptides, including C31, are potent enhancers of neuronal  
 CC apoptosis (By similarity).  
 CC -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several  
 CC cytoplasmic proteins, including APBB family members, the APBA  
 CC family, MAPK8IP1, SHC1 and Numb and Dab1 (By similarity). Also  
 CC interacts with GPCR-like protein BPP, FPRL1, APPBP1, IB1, KNS2  
 CC (via its TPR domains), APPBP2 (via BaSS) and DDB1 (By similarity).  
 CC Associates with microtubules in the presence of ATP and in a  
 CC kinesin-dependent manner (By similarity). Soluble Abeta40 binds  
 CC all three isoforms of APOE, in vitro and in vivo. When lipidated,  
 CC ApoE3 appears to be the preferred amyloid binding isoform, while  
 CC the apoE4 isoform-beta-APP40 complex is capable of being  
 CC transported across the blood-brain barrier.  
 CC -!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface  
 CC protein that rapidly becomes internalized via clathrin-coated pits  
 CC (By similarity). During maturation, the immature APP (N-  
 CC glycosylated in the endoplasmic reticulum) moves to the Golgi  
 CC complex where complete maturation occurs (O-glycosylated and  
 CC sulfated) (By similarity). After alpha-secretase cleavage, soluble  
 CC APP is released into the extracellular space and the C-terminal is  
 CC internalized to endosomes and lysosomes (By similarity). Some APP  
 CC accumulates in secretory transport vesicles leaving the late Golgi  
 CC compartment and returns to the cell surface (By similarity). APP  
 CC sorts to the basolateral surface in epithelial cells (By  
 CC similatity).  
 CC -!- ALTERNATIVE PRODUCTS:  
 CC Event=Alternative splicing; Named isoforms=2;  
 CC Comment=Additional isoforms, missing exons 7,8 and 15, seem to  
 CC exist. The L-isoforms, missing exon 15, are referred to as  
 CC appicans;  
 CC Name=APP770;  
 CC IsoId=Q60495-1; Sequence=Displayed;  
 CC Name=APP695;  
 CC IsoId=Q60495-2; Sequence=VSP\_007221, VSP\_007222;  
 CC -!- TISSUE SPECIFICITY: Isoform APP695 is the major isoform found in  
 CC brain. The longer isoforms containing the BPTI domain are  
 CC predominantly expressed in peripheral organs such as muscle and  
 CC liver.  
 CC -!- INDUCTION: Increased levels during neuronal differentiation.  
 CC -!- DOMAIN: The basolateral sorting signal (BaSS) is required for  
 CC sorting of membrane proteins to the basolateral surface of  
 CC epithelial cells.  
 CC -!- DOMAIN: The NPXY sequence motif found in many tyrosine-  
 CC phosphorylated proteins is required for the specific binding of

CC the PID domain. However additional amino acids either N- or C-  
 CC terminal to the NPXY motif are often required for complete  
 CC interaction. The PID domain-containing proteins which bind APP  
 CC require the YENPTY motif for full interaction. These interactions  
 CC are independent of phosphorylation on the terminal tyrosine  
 CC residue (By similarity). The NPXY site is also involved in  
 CC clathrin-mediated endocytosis.

- CC -!- PTM: Proteolytically processed under normal cellular conditions.  
 CC Cleavage by alpha-secretase or alternatively by beta-secretase  
 CC leads to generation and extracellular release of soluble APP  
 CC peptides, S-APP-alpha and S-APP-beta, respectively, and the  
 CC retention of corresponding membrane-anchored C-terminal fragments,  
 CC CTF-alpha and CTF-beta. Subsequent processing of CTF-alpha by  
 CC gamma-secretase yields P3 peptides. This is the major secretory  
 CC pathway and is nonamyloidogenic. Alternatively,  
 CC presenilin/nicastrin-mediated gamma-secretase processing of CTF-  
 CC beta releases the amyloid beta proteins, amyloid-beta 40 (Abeta40)  
 CC and amyloid-beta 42 (Abeta42), major components of amyloid  
 CC plaques, and the corresponding cytotoxic C-terminal fragments  
 CC (CTFs).
- CC -!- PTM: Proteolytically cleaved by caspase-3 during neuronal  
 CC apoptosis (By similarity).
- CC -!- PTM: N- and O-glycosylated. O-linkage of chondroitin sulfate to  
 CC the L-APP isoforms produces the APP proteoglycan core proteins,  
 CC the appicans (By similarity).
- CC -!- PTM: Phosphorylation in the C-terminal on tyrosine, threonine and  
 CC serine residues is neuron-specific (By similarity).  
 CC Phosphorylation can affect APP processing, neuronal  
 CC differentiation and interaction with other proteins.
- CC -!- PTM: Extracellular binding and reduction of copper, results in a  
 CC corresponding oxidation of Cys-144 and Cys-158, and the formation  
 CC of a disulfide bond (By similarity).
- CC -!- MISCELLANEOUS: Chelation of metal ions, notably copper, iron and  
 CC zinc, can induce histidine-bridging between beta-amyloid molecules  
 CC resulting in beta-amyloid-metal aggregates.
- CC -!- SIMILARITY: Belongs to the APP family.
- CC -!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.

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 CC -----

DR EMBL; X97631; CAA66230.1; -.  
 DR EMBL; X99198; CAA67589.1; -.  
 DR HSSP; P05067; 1BA4.  
 DR InterPro; IPR008155; A4\_APP.  
 DR InterPro; IPR008154; A4\_extra.  
 DR InterPro; IPR002223; Kunitz\_BPTI.  
 DR Pfam; PF00014; Kunitz\_BPTI; 1.  
 DR PRINTS; PR00203; AMYLOIDA4.  
 DR PRINTS; PR00759; BASICPTASE.  
 DR ProDom; PD000222; Kunitz\_BPTI; 1.  
 DR SMART; SM00006; A4\_EXTRA; 1.

DR SMART; SM00131; KU; 1.  
 DR PROSITE; PS00319; A4\_EXTRA; 1.  
 DR PROSITE; PS00320; A4\_INTRA; 1.  
 DR PROSITE; PS00280; BPTI\_KUNITZ\_1; 1.  
 DR PROSITE; PS50279; BPTI\_KUNITZ\_2; 1.  
 KW Apoptosis; Endocytosis; Cell adhesion; Serine protease inhibitor;  
 KW Coated pits; Neurone; Heparin-binding; Metal-binding; Copper; Iron;  
 KW Zinc; Signal; Transmembrane; Glycoprotein; Phosphorylation;  
 KW Proteoglycan; Alternative splicing; Amyloid.  
 FT SIGNAL 1 17 BY SIMILARITY.  
 FT CHAIN 18 770 AMYLOID BETA A4 PROTEIN.  
 FT CHAIN 18 687 SOLUBLE APP-ALPHA (BY SIMILARITY).  
 FT CHAIN 18 671 SOLUBLE APP-BETA (BY SIMILARITY).  
 FT CHAIN 672 770 CTF-ALPHA (BY SIMILARITY).  
 FT CHAIN 672 713 BETA-AMYLOID PROTEIN 42 (BY SIMILARITY).  
 FT CHAIN 672 711 BETA-AMYLOID PROTEIN 40 (BY SIMILARITY).  
 FT CHAIN 688 770 CTF-BETA (BY SIMILARITY).  
 FT CHAIN 688 713 P3(42) (BY SIMILARITY).  
 FT CHAIN 688 711 P3(40) (BY SIMILARITY).  
 FT CHAIN 712 770 GAMMA-CTF(59) (BY SIMILARITY).  
 FT CHAIN 714 770 GAMMA-CTF(57) (BY SIMILARITY).

Query Match 96.3%; Score 3514.5; DB 1; Length 770;  
 Best Local Similarity 87.9%; Pred. No. 3.8e-165;  
 Matches 677; Conservative 8; Mismatches 10; Indels 75; Gaps 1;

Qy 1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60  
 ||| ||||| |||||||||||||||||||||||||:|||||||||: |||||  
 Db 1 MLPSLALLLLTTWTARALEVPTDGNAGLLAEPQIAMFCGKLNHMNMNVQNGKWEPPDPSGTK 60  
 Qy 61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVPIPYRCLVG 120  
 ||| :||||||||||||||||||||||||||||||||||||| |||||||||||||||||  
 Db 61 TCIGSKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRSRKQCKTHPHFVPIPYRCLVG 120  
 Qy 121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180  
 |||||||||||||||||||||||||||||||||||||||  
 Db 121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180  
 Qy 181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240  
 |||||||||||||||:|||||||||||||||||:|||||  
 Db 181 GVEFVCCPLAEESDNIDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVADVVEE 240  
 Qy 241 EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVR----- 288  
 ||||| |||||||||||||||:|||||||||||||||  
 Db 241 EADDDDEDGDEVEEEAEPEYEEATEKTTSIATTTTTTTESVEEVVREVCSEQAETGPC 300  
 Qy 289 ----- 288  
 Db 301 RSMISRWFYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMVCGSVMSQNLLKTSGEVPSQG 360  
 Qy 289 ---VPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQA 345  
 :|||||||||||||||||||||||||||||||||||||  
 Db 361 PVKLPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQA 420  
 Qy 346 KNLPKADKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITAL 405  
 |||||||||||||||||||||||||||||||||||  
 Db 421 KNLPKADKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITAL 480

Qy 406 QAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYER 465  
 |||  
 Db 481 QAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYER 540  
 Qy 466 MNQSLSLLYNVPAAVEEQDEVDLLQKEQNYSDVLANMISEPRISYGNDAIMPSTET 525  
 |||  
 Db 541 MNQSLSLLYNVPAAVEEQDEVDLLQKEQNYSDVLANMISEPRISYGNDAIMPSTET 600  
 Qy 526 KTTVELLPVNGEFSDDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTN 585  
 |||  
 Db 601 KTTVELLPVNGEFSDDLQPWHPFGVDSVPANTENEVEPVDARPAADRGLTTRPGSGLTN 660  
 Qy 586 IKTEEISEVNLDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITL 645  
 ||| : |||  
 Db 661 IKTEEISEVKMDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITL 720  
 Qy 646 VMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695  
 |||  
 Db 721 VMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 770

# RESULT 6

## A4\_MOUSE

ID A4\_MOUSE STANDARD; PRT; 770 AA.  
 AC P12023; P97487; P97942; Q99K32;  
 DT 01-OCT-1989 (Rel. 12, Created)  
 DT 10-OCT-2003 (Rel. 42, Last sequence update)  
 DT 10-OCT-2003 (Rel. 42, Last annotation update)  
 DE Amyloid beta A4 protein precursor (APP) (ABPP) (Alzheimer's disease  
 DE amyloid protein homolog) (Amyloidogenic glycoprotein) (AG) [Contains:  
 DE Soluble APP-alpha (S-APP-alpha); Soluble APP-beta (S-APP-beta); C99  
 DE (APP-C99); Beta-amyloid protein 42 (Beta-APP42); Beta-amyloid protein  
 DE 40 (Beta-APP40); C83; P3(42); P3(40); Gamma-CTF(59) (Gamma-secretase  
 DE C-terminal fragment 59) (Amyloid intracellular domain 59) (AID(59))  
 DE (APP-C59); Gamma-CTF(57) (Gamma-secretase C-terminal fragment 57)  
 DE (Amyloid intracellular domain 57) (AID(57)) (APP-C57); Gamma-CTF(50)  
 DE (Gamma-secretase C-terminal fragment 50) (Amyloid intracellular domain  
 DE 50) (AID(50)); C31].  
 GN APP.  
 OS Mus musculus (Mouse).  
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
 OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.  
 OX NCBI\_TaxID=10090;  
 RN [1]  
 RP SEQUENCE FROM N.A. (ISOFORM APP695).  
 RC TISSUE=Brain;  
 RX MEDLINE=88106489; PubMed=3322280;  
 RA Yamada T., Sasaki H., Furuya H., Miyata T., Goto I., Sakaki Y.;  
 RT "Complementary DNA for the mouse homolog of the human amyloid beta  
 RT protein precursor";  
 RL Biochem. Biophys. Res. Commun. 149:665-671(1987).  
 RN [2]  
 RP REVISIONS.  
 RA Yamada T.;  
 RL Submitted (MAR-1988) to the EMBL/GenBank/DDBJ databases.  
 RN [3]

RP SEQUENCE FROM N.A. (ISOFORM APP695).  
 RC STRAIN=BALB/c; TISSUE=Brain;  
 RX MEDLINE=92096458; PubMed=1756177;  
 RA de Strooper B., van Leuven F., van den Berghe H.;  
 RT "The amyloid beta protein precursor or proteinase nexin II from mouse  
 RT is closer related to its human homolog than previously reported.";  
 RL Biochim. Biophys. Acta 1129:141-143(1991).  
 RN [4]

RP SEQUENCE FROM N.A. (ISOFORM APP695).  
 RC STRAIN=SAMP8; TISSUE=Hippocampus;  
 RX MEDLINE=21130647; PubMed=11235921;  
 RA Kumar V.B., Vyas K., Franko M., Choudhary V., Buddhiraju C.,  
 RA Alvarez J., Morley J.E.;  
 RT "Molecular cloning, expression, and regulation of hippocampal amyloid  
 RT precursor protein of senescence accelerated mouse (SAMP8).";  
 RL Biochem. Cell Biol. 79:57-67(2001).  
 RN [5]

RP SEQUENCE OF 1-19 FROM N.A.  
 RX MEDLINE=92209998; PubMed=1555768;  
 RA Izumi R., Yamada T., Yoshikai S.I., Sasaki H., Hattori M.,  
 RA Sakai Y.;  
 RT "Positive and negative regulatory elements for the expression of the  
 RT Alzheimer's disease amyloid precursor-encoding gene in mouse.";  
 RL Gene 112:189-195(1992).  
 RN [6]

RP PARTIAL SEQUENCE FROM N.A. (ISOFORM APP770).  
 RC TISSUE=Breast tumor;  
 RX MEDLINE=22388257; PubMed=12477932;  
 RA Strausberg R.L., Feingold E.A., Grouse L.H., Derge J.G.,  
 RA Klausner R.D., Collins F.S., Wagner L., Shenmen C.M., Schuler G.D.,  
 RA Altschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., Bhat N.K.,  
 RA Hopkins R.F., Jordan H., Moore T., Max S.I., Wang J., Hsieh F.,  
 RA Diatchenko L., Marusina K., Farmer A.A., Rubin G.M., Hong L.,  
 RA Stapleton M., Soares M.B., Bonaldo M.F., Casavant T.L., Scheetz T.E.,  
 RA Brownstein M.J., Usdin T.B., Toshiyuki S., Carninci P., Prange C.,  
 RA Raha S.S., Loquellano N.A., Peters G.J., Abramson R.D., Mullahy S.J.,  
 RA Bosak S.A., McEwan P.J., McKernan K.J., Malek J.A., Gunaratne P.H.,  
 RA Richards S., Worley K.C., Hale S., Garcia A.M., Gay L.J., Hulyk S.W.,  
 RA Villalon D.K., Muzny D.M., Sodergren E.J., Lu X., Gibbs R.A.,  
 RA Fahey J., Helton E., Kettelman M., Madan A., Rodrigues S., Sanchez A.,  
 RA Whiting M., Madan A., Young A.C., Shevchenko Y., Bouffard G.G.,  
 RA Blakesley R.W., Touchman J.W., Green E.D., Dickson M.C.,  
 RA Rodriguez A.C., Grimwood J., Schmutz J., Myers R.M.,  
 RA Butterfield Y.S.N., Krzywinski M.I., Skalska U., Smailus D.E.,  
 RA Schnerch A., Schein J.E., Jones S.J.M., Marra M.A.;  
 RT "Generation and initial analysis of more than 15,000 full-length human  
 RT and mouse cDNA sequences.";  
 RL Proc. Natl. Acad. Sci. U.S.A. 99:16899-16903(2002).  
 RN [7]

RP SEQUENCE OF 281-380 FROM N.A., AND ALTERNATIVE SPLICING.  
 RC TISSUE=Brain, and Kidney;  
 RX MEDLINE=89149813; PubMed=2493250;  
 RA Yamada T., Sasaki H., Dohura K., Goto I., Sakaki Y.;  
 RT "Structure and expression of the alternatively-spliced forms of mRNA  
 RT for the mouse homolog of Alzheimer's disease amyloid beta protein  
 RT precursor.";  
 RL Biochem. Biophys. Res. Commun. 158:906-912(1989).

RN [8]  
 RP SEQUENCE OF 289-364 FROM N.A.  
 RC STRAIN=CD-1; TISSUE=Placenta;  
 RX MEDLINE=89345111; PubMed=2569710;  
 RA Fukuchi K., Martin G.M., Deeb S.S.;  
 RT "Sequence of the protease inhibitor domain of the A4 amyloid protein  
 RT precursor of *Mus domesticus*.";  
 RL Nucleic Acids Res. 17:5396-5396(1989).  
 RN [9]  
 RP SEQUENCE OF 656-737 FROM N.A.  
 RC STRAIN=129/Sv;  
 RA Wragg M.A., Busfield F., Duff K., Korenblat K., Capecchi M.,  
 RA Loring J.F., Goate A.M.;  
 RT "Introduction of six mutations into the mouse genome using 'Hit and  
 RT Run' gene-targeting: introduction of familial Alzheimer's disease  
 RT mutations into the mouse amyloid precursor protein gene and  
 RT humanization of the A-beta fragment.";  
 RL Submitted (DEC-1996) to the EMBL/GenBank/DDBJ databases.  
 RN [10]  
 RP TISSUE SPECIFICITY OF ALTERNATIVE SPLICED FORMS.  
 RX MEDLINE=93287808; PubMed=8510506;  
 RA Sola C., Mengod G., Ghetti B., Palacios J.M., Triarhou L.C.;  
 RT "Regional distribution of the alternatively spliced isoforms of beta  
 RT APP RNA transcript in the brain of normal, heterozygous and  
 RT homozygous weaver mutant mice as revealed by in situ hybridization  
 RT histochemistry.";  
 RL Brain Res. Mol. Brain Res. 17:340-346(1993).  
 RN [11]  
 RP INTERACTION WITH KNS2.  
 RX MEDLINE=21010507; PubMed=11144355;  
 RA Kamal A., Stokin G.B., Yang Z., Xia C.-H., Goldstein L.S.;  
 RT "Axonal transport of amyloid precursor protein is mediated by direct  
 RT binding to the kinesin light chain subunit of kinesin-I.";  
 RL Neuron 28:449-459(2000).  
 RN [12]  
 RP C-TERMINAL PROTEIN-PROTEIN INTERACTIONS, AND MUTAGENESIS OF TYR-728;  
 RP THR-743; TYR-757; ASN-759 AND TYR-762.  
 RX MEDLINE=21408156; PubMed=11517249;  
 RA Matsuda S., Yasukawa T., Homma Y., Ito Y., Niikura T., Hiraki T.,  
 RA Hirai S., Ohno S., Kita Y., Kawasumi M., Kouyama K., Yamamoto T.,  
 RA Kyriakis J.M., Nishimoto I.;  
 RT "C-jun N-terminal kinase (JNK)-interacting protein-1b/islet-brain-1  
 RT scaffolds Alzheimer's amyloid precursor protein with JNK.";  
 RL J. Neurosci. 21:6597-6607(2001).  
 RN [13]  
 RP INTERACTION WITH MAPK8IP1, AND PHOSPHORYLATION.  
 RX MEDLINE=22028091; PubMed=11912189;  
 RA Taru H., Iijima K.-I., Hase M., Kirino Y., Yagi Y., Suzuki T.;  
 RT "Interaction of Alzheimer's beta-amyloid precursor family proteins  
 RT with scaffold proteins of the JNK signaling cascade.";  
 RL J. Biol. Chem. 277:20070-20078(2002).  
 RN [14]  
 RP INTERACTION OF CTF PEPTIDES WITH NUMB.  
 RX MEDLINE=22008109; PubMed=12011466;  
 RA Roncarati R., Sestan N., Scheinfeld M.H., Berechid B.E., Lopez P.A.,  
 RA Meucci O., McGlade J.C., Rakic P., D'Adamio L.;  
 RT "The gamma-secretase-generated intracellular domain of beta-amyloid

RT precursor protein binds Numb and inhibits Notch signaling.";  
 RL Proc. Natl. Acad. Sci. U.S.A. 99:7102-7107(2002).  
 RN [15]  
 RP GAMMA-SECRETASE PROCESSING, AND INTERACTION WITH APBB1.  
 RX MEDLINE=21437805; PubMed=11553691;  
 RA Cupers P., Orlans I., Craessaerts K., Annaert W., De Strooper B.;  
 RT "The amyloid precursor protein (APP)-cytoplasmic fragment generated by  
 RT gamma-secretase is rapidly degraded but distributes partially in a  
 RT nuclear fraction of neurones in culture.";  
 RL J. Neurochem. 78:1168-1178(2001).  
 CC -!- FUNCTION: Functions as a cell surface receptor and performs  
 CC physiological functions on the surface of neurons relevant to  
 CC neurite growth, neuronal adhesion and axonogenesis. Involved in  
 CC cell mobility and transcription regulation through protein-protein  
 CC interactions. Can promote transcription activation through binding  
 CC to APBB1/Tip60 and inhibit Notch signaling through interaction  
 CC with Numb. Couples to apoptosis-inducing pathways such as those  
 CC mediated by G(O) and JIP. Inhibits G(0) alpha ATPase activity (By  
 CC similarity). Acts as a kinesin I membrane receptor, mediating the  
 CC axonal transport of beta-secretase and presenilin 1. May be  
 CC involved in copper homeostasis/oxidative stress through copper ion  
 CC reduction. Can regulate neurite outgrowth through binding to  
 CC components of the extracellular matrix such as heparin and  
 CC collagen I and IV (By similarity). The splice isoforms that  
 CC contain the BPTI domain possess protease inhibitor activity (By  
 CC similarity).  
 CC -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators  
 CC with metal-reducing activity. Bind transient metals such as  
 CC copper, zinc and iron. Rat and mouse beta-amyloid peptides bind  
 CC only weakly transient metals and have little reducing activity due  
 CC to substitutions of transient metal chelating residues. Beta-APP42  
 CC may activate mononuclear phagocytes in the brain and elicit  
 CC inflammatory responses. Promotes both tau aggregation and TPK II-  
 CC mediated phosphorylation (By similarity).  
 CC -!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved  
 CC peptides, including C31, are potent enhancers of neuronal  
 CC apoptosis.  
 CC -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several  
 CC cytoplasmic proteins, including APBB family members, the APBA  
 CC family, MAPK8IP1, SHC1, Numb and Dab1. Binding to Dab1 inhibits  
 CC its serine phosphorylation. Also interacts with GPCR-like protein  
 CC BPP, FPRL1, APPBP1, IB1, KNS2 (via its TPR domains), APPBP2 (via  
 CC BaSS) and DDB1 (By similarity). In vitro, it binds MAPT via the  
 CC MT-binding domains (By similarity). Associates with microtubules  
 CC in the presence of ATP and in a kinesin-dependent manner (By  
 CC similarity). Interacts, through a C-terminal domain, with GNAO1  
 CC (By similarity). Amyloid beta-42 binds CHRNA7 in hippocampal  
 CC neurons (By similarity). Beta-amyloid associates with HADH2 (By  
 CC similarity).  
 CC -!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface  
 CC protein that rapidly becomes internalized via clathrin-coated  
 CC pits. During maturation, the immature APP (N-glycosylated in the  
 CC endoplasmic reticulum) moves to the Golgi complex where complete

Query Match 95.5%; Score 3485.5; DB 1; Length 770;  
 Best Local Similarity 87.5%; Pred. No. 1e-163;  
 Matches 674; Conservative 7; Mismatches 14; Indels 75; Gaps 1;





AC P08592;  
 DT 01-AUG-1988 (Rel. 08, Created)  
 DT 01-DEC-1992 (Rel. 24, Last sequence update)  
 DT 10-OCT-2003 (Rel. 42, Last annotation update)  
 DE Amyloid beta A4 protein precursor (APP) (Alzheimer's disease amyloid  
 DE protein homolog) (Amyloidogenic glycoprotein) (AG) [Contains: Soluble  
 DE APP-alpha (S-APP-alpha); Soluble APP-beta (S-APP-beta); C99; Beta-  
 DE amyloid protein 42 (Beta-APP42); Beta-amyloid protein 40 (Beta-APP40);  
 DE C83; P3(42); P3(40); Gamma-CTF(59) (Gamma-secretase C-terminal  
 DE fragment 59); Gamma-CTF(57) (Gamma-secretase C-terminal fragment 57);  
 DE Gamma-CTF(50) (Gamma-secretase C-terminal fragment 50); C31].  
 GN APP.  
 OS Rattus norvegicus (Rat).  
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
 OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Rattus.  
 OX NCBI\_TaxID=10116;  
 RN [1]  
 RP SEQUENCE FROM N.A. (ISOFORM APP695).  
 RC TISSUE=Brain;  
 RX MEDLINE=88312583; PubMed=2900758;  
 RA Shivers B.D., Hilbich C., Multhaup G., Salbaum J.M., Beyreuther K.,  
 RA Seeburg P.H.;  
 RT "Alzheimer's disease amyloidogenic glycoprotein: expression pattern  
 RT in rat brain suggests a role in cell contact.";  
 RL EMBO J. 7:1365-1370(1988).  
 RN [2]  
 RP SEQUENCE OF 289-364 FROM N.A.  
 RC TISSUE=Liver;  
 RX MEDLINE=89183625; PubMed=2648331;  
 RA Kang J., Mueller-Hill B.;  
 RT "The sequence of the two extra exons in rat preA4.";  
 RL Nucleic Acids Res. 17:2130-2130(1989).  
 RN [3]  
 RP SEQUENCE OF 720-730, AND MASS SPECTROMETRY.  
 RX MEDLINE=21443797; PubMed=11483588;  
 RA Gu Y., Misonou H., Sato T., Dohmae N., Takio K., Ihara Y.;  
 RT "Distinct intramembrane cleavage of the beta-amyloid precursor protein  
 RT family resembling gamma-secretase-like cleavage of Notch.";  
 RL J. Biol. Chem. 276:35235-35238(2001).  
 RN [4]  
 RP ALTERNATIVE SPLICING.  
 RX MEDLINE=96187032; PubMed=8624099;  
 RA Sandbrink R., Masters C.L., Beyreuther K.;  
 RT "APP gene family. Alternative splicing generates functionally related  
 RT isoforms.";  
 RL Ann. N.Y. Acad. Sci. 777:281-287(1996).  
 RN [5]  
 RP TISSUE SPECIFICITY OF APPICAN.  
 RX MEDLINE=95263526; PubMed=7744833;  
 RA Shioi J., Pangalos M.N., Ripellino J.A., Vassilacopoulou D.,  
 RA Mytilineou C., Margolis R.U., Robakis N.K.;  
 RT "The Alzheimer amyloid precursor proteoglycan (appican) is present in  
 RT brain and is produced by astrocytes but not by neurons in primary  
 RT neural cultures.";  
 RL J. Biol. Chem. 270:11839-11844(1995).  
 RN [6]  
 RP TISSUE SPECIFICITY OF ISOFORMS.

RX MEDLINE=97150061; PubMed=8996834;  
 RA Sandbrink R., Monning U., Masters C.L., Beyreuther K.;  
 RT "Expression of the APP gene family in brain cells, brain development  
 RT and aging.";  
 RL Gerontology 43:119-131(1997).  
 RN [7]  
 RP INTERACTION WITH DDB1, AND MUTAGENESIS OF TYR-757; ASN-759 AND  
 RP TYR-762.  
 RX MEDLINE=99127916; PubMed=9930726;  
 RA Watanabe T., Sukegawa J., Tomita S., Iijima K.-I., Oguchi S.,  
 RA Suzuki T., Nairn A.C., Greengard P.;  
 RT "A 127-kDa protein (UV-DDB) binds to the cytoplasmic domain of the  
 RT Alzheimer's amyloid precursor protein.";  
 RL J. Neurochem. 72:549-556(1999).  
 RN [8]  
 RP INTERACTION WITH GNAO1, AND MUTAGENESIS OF 732-HIS-HIS-733.  
 RX MEDLINE=99162676; PubMed=10024358;  
 RA Brouillet E., Trembleau A., Galanaud D., Volovitch M., Bouilliot C.,  
 RA Valenza C., Prochiantz A., Allinquant B.;  
 RT "The amyloid precursor protein interacts with Go heterotrimeric  
 RT protein within a cell compartment specialized in signal  
 RT transduction.";  
 RL J. Neurosci. 19:1717-1727(1999).  
 RN [9]  
 RP CHARACTERISTICS OF APPICAN, AND MUTAGENESIS OF SER-656.  
 RX MEDLINE=95256193; PubMed=7737970;  
 RA Pangalos M.N., Efthimiopoulos S., Shioi J., Robakis N.K.;  
 RT "The chondroitin sulfate attachment site of appican is formed by  
 RT splicing out exon 15 of the amyloid precursor gene.";  
 RL J. Biol. Chem. 270:10388-10391(1995).  
 RN [10]  
 RP BETA-AMYLOID METAL-BINDING.  
 RX MEDLINE=99316162; PubMed=10386999;  
 RA Huang X., Atwood C.S., Hartshorn M.A., Multhaup G., Goldstein L.E.,  
 RA Scarpa R.C., Cuajungco M.P., Gray D.N., Lim J., Moir R.D., Tanzi R.E.,  
 RA Bush A.I.;  
 RT "The A beta peptide of Alzheimer's disease directly produces hydrogen  
 RT peroxide through metal ion reduction.";  
 RL Biochemistry 38:7609-7616(1999).  
 RN [11]  
 RP BETA-AMYLOID ZINC BINDING.  
 RX MEDLINE=99343552; PubMed=10413512;  
 RA Liu S.T., Howlett G., Barrow C.J.;  
 RT "Histidine-13 is a crucial residue in the zinc ion-induced aggregation  
 RT of the A beta peptide of Alzheimer's disease.";  
 RL Biochemistry 38:9373-9378(1999).  
 RN [12]  
 RP IMPORTANCE OF GLY-704 IN FREE RADICAL PROPAGATION, AND MUTAGENESIS OF  
 RP GLY-704.  
 RX MEDLINE=21956095; PubMed=11959460;  
 RA Kanski J., Varadarajan S., Aksenova M., Butterfield D.A.;  
 RT "Role of glycine-33 and methionine-35 in Alzheimer's amyloid beta-  
 RT peptide 1-42-associated oxidative stress and neurotoxicity.";  
 RL Biochim. Biophys. Acta 1586:190-198(2001).  
 RN [13]  
 RP PHOSPHORYLATION.  
 RX MEDLINE=97239592; PubMed=9085254;

RA Oishi M., Nairn A.C., Czernik A.J., Lim G.S., Isohara T., Gandy S.E.,  
 RA Greengard P., Suzuki T.;  
 RT "The cytoplasmic domain of Alzheimer's amyloid precursor protein is  
 RT phosphorylated at Thr654, Ser655, and Thr668 in adult rat brain and  
 RT cultured cells.";  
 RL Mol. Med. 3:111-123(1997).  
 RN [14]  
 RP PHOSPHORYLATION ON SER-730.  
 RX MEDLINE=99262094; PubMed=10329382;  
 RA Isohara T., Horiuchi A., Watanabe T., Ando K., Czernik A.J., Uno I.,  
 RA Greengard P., Nairn A.C., Suzuki T.;  
 RT "Phosphorylation of the cytoplasmic domain of Alzheimer's beta-amyloid  
 RT precursor protein at Ser655 by a novel protein kinase.";  
 RL Biochem. Biophys. Res. Commun. 258:300-305(1999).  
 RN [15]  
 RP PHOSPHORYLATION, INDUCTION, SUBCELLULAR LOCATION, AND MUTAGENESIS OF  
 RP THR-743.  
 RX MEDLINE=99274744; PubMed=10341243;  
 RA Ando K., Oishi M., Takeda S., Iijima K.-I., Isohara T., Nairn A.C.,  
 RA Kirino Y., Greengard P., Suzuki T.;  
 RT "Role of phosphorylation of Alzheimer's amyloid precursor protein  
 RT during neuronal differentiation.";  
 RL J. Neurosci. 19:4421-4427(1999).  
 RN [16]  
 RP PHOSPHORYLATION ON THR-743.  
 RX MEDLINE=20396183; PubMed=10936190;  
 RA Iijima K.-I., Ando K., Takeda S., Satoh Y., Seki T., Itohara S.,  
 RA Greengard P., Kirino Y., Nairn A.C., Suzuki T.;  
 RT "Neuron-specific phosphorylation of Alzheimer's beta-amyloid precursor  
 RT protein by cyclin-dependent kinase 5.";  
 RL J. Neurochem. 75:1085-1091(2000).  
 RN [17]  
 RP CARBOHYDRATE STRUCTURE OF APPICAN.  
 RX MEDLINE=21463085; PubMed=11479316;  
 RA Tsuchida K., Shioi J., Yamada S., Boghosian G., Wu A., Cai H.,  
 RA Sugahara K., Robakis N.K.;  
 RT "Appican, the proteoglycan form of the amyloid precursor protein,  
 RT contains chondroitin sulfate E in the repeating disaccharide region  
 RT and 4-O-sulfated galactose in the linkage region.";  
 RL J. Biol. Chem. 276:37155-37160(2001).  
 CC -!- FUNCTION: Functions as a cell surface receptor and performs  
 CC physiological functions on the surface of neurons relevant to  
 CC neurite growth, neuronal adhesion and axonogenesis. Involved in  
 CC cell mobility and transcription regulation through protein-protein  
 CC interactions (By similarity). Can promote transcription activation  
 CC through binding to APBB1/Tip60 and inhibit Notch signaling through  
 CC interaction with Numb (By similarity). Couples to apoptosis-  
 CC inducing pathways such as those mediated by G(O) and JIP. Inhibits  
 CC G(O) alpha ATPase activity. Acts as a kinesin I membrane receptor,  
 CC mediating the axonal transport of beta-secretase and presenilin 1  
 CC (By similarity). May be involved in copper homeostasis/oxidative  
 CC stress through copper ion reduction. Can regulate neurite  
 CC outgrowth through binding to components of the extracellular  
 CC matrix such as heparin and collagen I and IV (By similarity). The  
 CC splice isoforms that contain the BPTI domain possess protease  
 CC inhibitor activity (By similarity).  
 CC -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators

CC with metal-reducing activity. Bind transient metals such as  
 CC copper, zinc and iron. Rat and mouse beta-amyloid peptides bind  
 CC only weakly transient metals and have little reducing activity due  
 CC to substitutions of transient metal chelating residues. Beta-APP42  
 CC may activate mononuclear phagocytes in the brain and elicit  
 CC inflammatory responses. Promotes both tau aggregation and TPK II-  
 CC mediated phosphorylation (By similarity).  
 CC -!- FUNCTION: Appicans elicit adhesion of neural cells to the  
 CC extracellular matrix and may regulate neurite outgrowth in the  
 CC brain.  
 CC -!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved  
 CC peptides, including C31, are potent enhancers of neuronal  
 CC apoptosis (By similarity).  
 CC -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several  
 CC cytoplasmic proteins, including APBB family members, the APBA  
 CC family, MAPK8IP1, SHC1 and Numb and Dab1 (By similarity). Binding  
 CC to Dab1 inhibits its serine phosphorylation (By similarity). Also  
 CC interacts with GPCR-like protein BPP, FPRL1, APPBP1, IB1, KNS2  
 CC (via its TPR domains), APPBP2 (via BaSS) (By similarity) and DDB1.  
 CC In vitro, it binds MAPT via the MT-binding domains (By  
 CC similarity). Associates with microtubules in the presence of ATP  
 CC and in a kinesin-dependent manner (By similarity). Interacts,  
 CC through a C-terminal domain, with GNAO1. Amyloid beta-42 binds  
 CC CHRNA7 in hippocampal neurons (By similarity). Beta-amyloid  
 CC associates with HADH2 (By similarity).  
 CC -!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface  
 CC protein that rapidly becomes internalized via clathrin-coated  
 CC pits. During maturation, the immature APP (N-glycosylated in the

Query Match 95.5%; Score 3485.5; DB 1; Length 770;  
 Best Local Similarity 87.4%; Pred. No. 1e-163;  
 Matches 673; Conservative 9; Mismatches 13; Indels 75; Gaps 1;

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Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
      ||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db      1 MLPSLALLLLAAWTVRALEVPTDGNAGLLAEPQIAMFCGKLNMHMNVQNGKWESDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
      ||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db     61 TCIGTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHTHIVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
      ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
      ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db    181 GVEFVCCPLAEESDSIDSADAEEDSDVWWGGADTDYADGGEDKVVEVAEEEEVADVVEEE 240

Qy    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTTSIATTTTTTTESVEEVVR----- 288
      ||:|||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db    241 EAEDDEDVEDGDEVEEEAEPEYEEATERTTTSIATTTTTTTESVEEVVREVCSEAETGPC 300

Qy    289 ----- 288

Db    301 RAMISRWFYFDVTEGKCAPFFYGGCGGNRRNFDTEEYCMVCGSVSSQSLLKTTSEPLPQD 360

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Qy	289	---VPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQA	345
		:	
Db	361	PVKLPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQA	420
Qy	346	KNLPKADKKAVIQHFQEKVESLEQEAAENERQQLVETHMARVEAMLNDRRLALENYITAL	405
Db	421	KNLPKADKKAVIQHFQEKVESLEQEAAENERQQLVETHMARVEAMLNDRRLALENYITAL	480
Qy	406	QAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYER	465
Db	481	QAVPPRPHHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYER	540
Qy	466	MNQSLSLLYNVPAAVEEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDALMPSLTET	525
Db	541	MNQSLSLLYNVPAAVEEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDALMPSLTET	600
Qy	526	KTTVELLPVNGEFSDDLQPWHSFGADSVANTENEVEPVDPARPAADRGLTTRPGSGLTN	585
Db	601	KTTVELLPVNGEFSDDLQPWHPFGVDSVPANTENEVEPVDPARPAADRGLTTRPGSGLTN	660
Qy	586	IKTEEISEVNLDAEFRHDSGYEVHQLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITL	645
		:    :	
Db	661	IKTEEISEVKMDAEFGHDSGFVHRHQLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITL	720
Qy	646	VMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN	695
Db	721	VMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN	770

RESULT 8

A4\_TETFL

ID A4\_TETFL STANDARD; PRT; 780 AA.

AC O73683;

DT 10-OCT-2003 (Rel. 42, Created)

DT 10-OCT-2003 (Rel. 42, Last sequence update)

DT 10-OCT-2003 (Rel. 42, Last annotation update)

DE Alzheimer's disease amyloid A4 protein homolog precursor [Contains:

DE Beta-amyloid protein (Beta-APP) (A-beta)].

GN APP.

OS Tetraodon fluviatilis (Puffer fish).

OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;

OC Actinopterygii; Neopterygii; Teleostei; Euteleostei; Neoteleostei;

OC Acanthomorpha; Acanthopterygii; Percomorpha; Tetraodontiformes;

OC Tetraodontoidea; Tetraodontidae; Tetraodon.

OX NCBI\_TaxID=47145;

RN [1]

RP SEQUENCE FROM N.A.

RX MEDLINE=98252138; PubMed=9599080;

RA Villard L., Tassone F., Crnogorac-Jurcevic T., Clancy K., Gardiner K.;

RT "Analysis of pufferfish homologues of the AT-rich human APP gene.";

RL Gene 210:17-24(1998).

CC !- FUNCTION: Functional neuronal receptor which couples to

CC intracellular signaling pathway through the GTP-binding protein

CC G(O) (By similarity).

CC !- SUBCELLULAR LOCATION: Type I membrane protein.

CC !- SIMILARITY: Belongs to the APP family.

CC !- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.



Db 128 LLVPDKCKFLHQERMNQCESHLHWHTVAKESCGDRAMNLHDYGMLLPCGIDRFRGVEFVC 187

Qy 187 CPLAEESDNVDSADAEEDSDVWVGADTDYADGS-----EDKVVEVAEEE 232  
 || || :|| : : ||||| ||:| | ||| ||

Db 188 CP-AEAERDMSTEKDADSDVWVGADNDYSDNSMVREPEPAEQQEETRPSVVEEEEG 246

Qy 233 EVAEVEEEE-----ADDEDEDGDEVEEEAEPEYEEATERTTSIA 273  
 |||: :|| | ||:| ||:| | :| | ||:|

Db 247 EVAQEDDEEEEVLDTDQDGDGEEDHEAADDEEEEDVDEIDAFGESDDVDADEPTTNVA 306

Qy 274 ---TTTTTTTESVEEVVR----- 288  
 |||||

Db 307 MTTTTTTTTTTTESVEEVVRMFCWAHADTGPCTASMPSWYFDAVDGRTMYELMYGGCGNMN 366

Qy 289 -----VPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQ 333  
 ||| |:|||| | ||| ||||| |||||

Db 367 NFESEYCLSVCSVVPDMPSSPDAVDHYLETADENEHAHFQKAKESLEAKHRERMSQ 426

Qy 334 VMREWEEAERQAKNLPKADKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDR 393  
 |||||:|||| || | |||:||||:|||||:|||||

Db 427 VMREWEEAERQAKNLPADKKIVIQRFQEKVEALEQEAASERQQLVETHMARVEALLNDR 486

Qy 394 RRLALENYITALQAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRS 453  
 |||||:|||| | |||||:|||||

Db 487 RRLALENYLTALQQDPPRPRHVFSLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRP 546

Qy 454 QVMTHLRVIYERMNQSLSLYNVPAVAEEIQDEVDLLQKEQNYSDDLANMISEPRISY 513  
 |:|||| | |||| | || || |:|:| | |||:| | |||: :| :|

Db 547 QVLTHLRVIEERMNQSLGLLYKVPGVADDIQDQV-ELLQREQAEMAQQLANLQTDVRVSY 605

Qy 514 GNDALMPSLTETKTTVELLPVNGEFLDDLQPDWH--SFGADSVPAANTENEVEPVDPARPA 571  
 ||||| :|| | :| : | || | |||:||||:|

Db 606 GNDALMPDQELGDGQADLLP--QEDTLGGVGFVHPESFN---QLNTENQVEPVDSRPTF 659

Qy 572 DRGLTTRPGSGLTNIKTEEISEVNLDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLM 631  
 :||: ||| :| | :| : :| | : |||||

Db 660 ERGVPTRP--VTGKSMEAVPELRMETEDRQSTEYEVHHQKLVFFAEDVGSNKGAIIGLM 716

Qy 632 VGGVVIATVIVITLVMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFE 691  
 |||||:|||||:|||||:|||||

Db 717 VGGVVIATVIVITLVMLRKKQYTSIHGGIIEVDAAVTPEERHLSKMQQNGYENPTYKFFE 776

Qy 692 QMQN 695  
 ||||

Db 777 QMQN 780

# RESULT 9

A4\_FUGRU

ID A4\_FUGRU STANDARD; PRT; 737 AA.

AC 093279;

DT 10-OCT-2003 (Rel. 42, Created)

DT 10-OCT-2003 (Rel. 42, Last sequence update)

DT 10-OCT-2003 (Rel. 42, Last annotation update)

DE Alzheimer's disease amyloid A4 protein homolog precursor [Contains:

DE Beta-amyloid protein (Beta-APP) (A-beta)].

GN APP.

OS Fugu rubripes (Japanese pufferfish) (Takifugu rubripes).  
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
 OC Actinopterygii; Neopterygii; Teleostei; Euteleostei; Neoteleostei;  
 OC Acanthomorpha; Acanthopterygii; Percomorpha; Tetraodontiformes;  
 OC Tetradontoidea; Tetraodontidae; Takifugu.  
 OX NCBI\_TaxID=31033;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RX MEDLINE=98252138; PubMed=9599080;  
 RA Villard L., Tassone F., Crnogorac-Jurcevic T., Clancy K., Gardiner K.;  
 RT "Analysis of pufferfish homologues of the AT-rich human APP gene.";  
 RL Gene 210:17-24(1998).  
 CC -!- FUNCTION: Functional neuronal receptor which couples to  
 CC intracellular signaling pathway through the GTP-binding protein  
 CC G(O) (By similarity).  
 CC -!- SUBCELLULAR LOCATION: Type I membrane protein.  
 CC -!- SIMILARITY: Belongs to the APP family.  
 CC -!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.  
 CC -----  
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 CC -----  
 DR EMBL; AF090120; AAD13392.1; -.  
 DR HSSP; P05067; 1HZ3.  
 DR InterPro; IPR008155; A4\_APP.  
 DR InterPro; IPR008154; A4\_extra.  
 DR InterPro; IPR001255; Beta-APP.  
 DR InterPro; IPR002223; Kunitz\_BPTI.  
 DR Pfam; PF02177; A4\_EXTRA; 1.  
 DR Pfam; PF03494; Beta-APP; 1.  
 DR Pfam; PF00014; Kunitz\_BPTI; 1.  
 DR PRINTS; PR00203; AMYLOIDA4.  
 DR PRINTS; PR00759; BASICPTASE.  
 DR ProDom; PD000222; Kunitz\_BPTI; 1.  
 DR SMART; SM00006; A4\_EXTRA; 1.  
 DR SMART; SM00131; KU; 1.  
 DR PROSITE; PS00319; A4\_EXTRA; FALSE\_NEG.  
 DR PROSITE; PS00320; A4\_INTRA; 1.  
 DR PROSITE; PS00280; BPTI\_KUNITZ\_1; 1.  
 DR PROSITE; PS50279; BPTI\_KUNITZ\_2; 1.  
 KW Glycoprotein; Amyloid; Neurone; Transmembrane; Signal;  
 KW Serine protease inhibitor.  
 FT SIGNAL 1 18 POTENTIAL.  
 FT CHAIN 19 737 ALZHEIMER'S DISEASE AMYLOID A4  
 FT PROTEIN HOMOLOG.  
 FT CHAIN 639 681 BETA-AMYLOID PROTEIN (POTENTIAL).  
 FT DOMAIN 19 668 EXTRACELLULAR (POTENTIAL).  
 FT TRANSMEM 669 689 POTENTIAL.  
 FT DOMAIN 690 737 CYTOPLASMIC (POTENTIAL).  
 FT DOMAIN 286 344 BPTI/KUNITZ INHIBITOR.  
 FT SITE 726 729 CLATHRIN-BINDING (BY SIMILARITY).  
 FT ACT\_SITE 300 301 REACTIVE BOND.



FT DISULFID 290 340 BY SIMILARITY.  
 FT DISULFID 299 323 BY SIMILARITY.  
 FT DISULFID 315 336 BY SIMILARITY.  
 FT CARBOHYD 522 522 N-LINKED (GLCNAC. . .) (POTENTIAL).  
 SQ SEQUENCE 737 AA; 82856 MW; 6FAD01E2E3B2B7E2 CRC64;

Query Match 67.0%; Score 2446.5; DB 1; Length 737;  
 Best Local Similarity 64.0%; Pred. No. 7e-113;  
 Matches 482; Conservative 83; Mismatches 101; Indels 87; Gaps 12;

Qy 7 LLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGKTCTIDTK 66  
 :||| | :| :| | ||| |||:||||:||||:|||||:|||||:|:|  
 Db 8 VLLLVATLRSSEIPADDTVGLLTPQVAMFCGKLNMHINVQNGKWESDPSGKTKSCLNTK 67

Qy 67 EGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVGEFVSDA 126  
 |||||:|||||:||||:| | |:|||||  
 Db 68 EGILQYCQEVPELQITNVVEANQPVSQNWCKKGRKQCRSHTHIVVPYRCLVGEFVSDA 127

Qy 127 LLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFRGVEFVC 186  
 |||||: ||:|||||:| ::| |||||:||||:|  
 Db 128 LLVPDKCKFLHQERMNQCESHLHWHTVAKESCGDRSMNLHDYGMLLPCGIDRFRGVKFVC 187

Qy 187 CPLAEESDNVDSADAEEDSDVWGGADTDYADGS---EDKVVEVAEEEEVAEEEEAD 243  
 || || ||:: | ::||| |||:|:| : ||: | :| |  
 Db 188 CP-AETEQETDSSEVEGEESDVWGGADPEYSENSPPTPSRATYVAGD---AFERDENG 243

Qy 244 DDEDEDGDEVEEEAEPYEEATERTTSIA--TTTTTTTESVEEVVR----- 288  
 |||:| :|: | :| ||| :| |||||  
 Db 244 GDEDEDEDVDPTDE---QESDERTANVAMTTTTTTTESVEEVVRVAVCWAQAESGPCR 300

Qy 289 -----VPTTAASTPDAVDKYLE 305  
 :|| | | |||:| |  
 Db 301 AMLERWYFNPKKRRCVPFLFGCGGNRNNFESEYCLAVCSSSLPTVAPSPPDQYFE 360

Qy 306 TPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHFQEKVE 365  
 |||:|||| |:||| |||||:|||||:|||||  
 Db 361 APGDDNEHADFRKAKESLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHFQEKVE 420

Qy 366 SLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLKKYVRA 425  
 :||||| |||||:| ||| |||: ||| ||| | | :|  
 Db 421 ALEQEAAAGERQQLVETHMARVEALLNSRRRLTLENYLGALQANPPRARQVLSLLKKYVRA 480

Qy 426 EQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAVAEEIQD 485  
 |||||:|||| ||||| ||:|||| |||||:| ||:| |||  
 Db 481 EQKDRQHTLKHFEHVRTVDPKKAAQIRPQVLTHLRVIDERMNQSLSLLYKVPVASEIQN 540

Qy 486 EVDELLQKEQNYSDDVLNMMIS---EPRISYGNDALMPSLTETKTTVELLPVNGEFLSDD 542  
 :: : | : : : : ||||| : : : | :| :|  
 Db 541 QIYPAAGSD---CKDPVEHCVCQVDGLVSYGNDALMPDQAYSSAPMD-MGVDGLGSID- 595

Qy 543 LQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLDAEFRH 602  
 || |||| ||||| ||| ||| :::| ||: || : : |  
 Db 596 ----QSFN----QANTENHVEPVDARPIPDRLPTRP---VSSLKLEEMPEVRTETDKRQ 644

Qy 603 DSGYEVHHQKLFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGVE 662  
 :||||:|||||:|||||:|||||:|||||:|||||:|  
 Db 645 SAGYEVYHQKLFFADDVGSNKGAIIGLMVGGVVIATVIVITLVMLLRKKQYTSIHGVIE 704

Qy            663 VDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695  
               |::|  
 Db            705 VDAAVTPEERHLARMQQNGYENPTYKFFEQMQN 737

RESULT 10

APP2\_MOUSE

ID APP2\_MOUSE            STANDARD;            PRT;    695 AA.  
 AC Q06335;  
 DT 01-JUN-1994 (Rel. 29, Created)  
 DT 01-FEB-1996 (Rel. 33, Last sequence update)  
 DT 15-MAR-2004 (Rel. 43, Last annotation update)  
 DE Amyloid-like protein 2 precursor (CDEI-box binding protein) (CDEBP).  
 GN APLP2.  
 OS Mus musculus (Mouse).  
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
 OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.  
 OX NCBI\_TaxID=10090;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RC TISSUE=Fetal brain;  
 RA von der Kammer H.;  
 RL Submitted (JUL-1994) to the EMBL/GenBank/DDBJ databases.  
 RN [2]  
 RP SEQUENCE OF 1-246 FROM N.A.  
 RX MEDLINE=94032480; PubMed=8218408;  
 RA Hanes J., von der Kammer H., Kristjansson G.I., Scheit K.H.;  
 RT "The complete cDNA coding sequence for the mouse CDEI binding  
 RT protein.";  
 RL Biochim. Biophys. Acta 1216:154-156(1993).  
 RN [3]  
 RP SEQUENCE OF 185-695 FROM N.A.  
 RC STRAIN=BALB/c; TISSUE=Heart;  
 RX MEDLINE=93129193; PubMed=1482349;  
 RA Vidal F., Blangy A., Rassoulzadegan M., Cuzin F.;  
 RT "A murine sequence-specific DNA binding protein shows extensive local  
 RT similarities to the amyloid precursor protein.";  
 RL Biochem. Biophys. Res. Commun. 189:1336-1341(1992).  
 RN [4]  
 RP SEQUENCE OF 1-35 FROM N.A.  
 RC STRAIN=129/Sv;  
 RX MEDLINE=96029629; PubMed=7592716;  
 RA von Koch C.S., Lahiri D.K., Mammen A.L., Copeland N.G.,  
 RA Gilbert D.J., Jenkins N.A., Sisodia S.S.;  
 RT "The mouse APLP2 gene. Chromosomal localization and promoter  
 RT characterization.";  
 RL J. Biol. Chem. 270:25475-25480(1995).  
 CC -!- FUNCTION: Binds to the DNA 5'-GTCACATG-3' (CDEI box) which plays  
 CC an important role in the early development of embryos.  
 CC -!- SUBCELLULAR LOCATION: Type I membrane protein and nuclear  
 CC (Potential).  
 CC -!- SIMILARITY: Belongs to the APP family.  
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CC -----  
DR EMBL; Z22592; CAA80306.1; -.  
DR EMBL; M97216; AAA20039.1; -.  
DR EMBL; U34291; AAC52318.1; -.  
DR PIR; JC1404; JC1404.  
DR PIR; S38344; S38344.  
DR HSSP; P05067; 1MWP.  
DR MGD; MGI:88047; Aplp2.  
DR InterPro; IPR008155; A4\_APP.  
DR InterPro; IPR008154; A4\_extra.  
DR Pfam; PF02177; A4\_EXTRA; 1.  
DR PRINTS; PR00203; AMYLOIDA4.  
DR SMART; SM00006; A4\_EXTRA; 1.  
DR PROSITE; PS00319; A4\_EXTRA; 1.  
DR PROSITE; PS00320; A4\_INTRA; 1.  
KW Transmembrane; DNA-binding; Signal; Nuclear protein.  
FT SIGNAL 1 29 POTENTIAL.  
FT CHAIN 30 695 AMYLOID-LIKE PROTEIN 2.  
FT DOMAIN 30 624 EXTRACELLULAR (POTENTIAL).  
FT TRANSMEM 625 648 POTENTIAL.  
FT DOMAIN 649 695 CYTOPLASMIC (POTENTIAL).  
FT DOMAIN 218 294 ASP/GLU-RICH (HIGHLY ACIDIC).  
FT DOMAIN 218 231 POLY-GLU.  
FT DOMAIN 256 266 POLY-GLU.  
FT CARBOHYD 485 485 N-LINKED (GLCNAC. . .) (POTENTIAL).  
FT CONFLICT 185 189 GMLLP -> MACCC (IN REF. 3).  
SQ SEQUENCE 695 AA; 78944 MW; BBF4B95AAB2A0311 CRC64;

Query Match 47.4%; Score 1730; DB 1; Length 695;  
Best Local Similarity 49.0%; Pred. No. 7.9e-78;  
Matches 358; Conservative 119; Mismatches 163; Indels 90; Gaps 19;

Qy 5 LALLLLAAWTARALEV-----PTDGNAG---LLAEPQIAMFCGR\_LNMHMNVQNGKWDSDP 56  
| :||| || | : ||| :||||| ||:||||:|:| |||: ||  
Db 15 LLVLLLLGLTAPAAALAGYIEALAANAGTGFAVAEPQIAMLCGK\_LNMHVNIQTGKWEPPD 74  
  
Qy 57 SGTKTCTIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYR 116  
:||||:| ||| :|||||:|||||:||||| | :||:| :|||: | |||:  
Db 75 TGTKSCLGTKEEV\_LQYCQEIYPELQITNVMEANQPVNIDSWCRRDKRQCKS--HIVIPFK 132  
  
Qy 117 CLVGEFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGM\_LLP CGI 176  
||||||| |||| | :| ||||:||| | |||: || | : | : |||||:  
Db 133 CLVGEFVSDVLLVPDNCQFFHQERMEVCEKHQRWHTLVKEACLTEGLTLYSYGM\_LLP CGV 192  
  
Qy 177 DKFRGVEFVCCPLAE--ESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAE---E 231  
|:| | |:|||| : :||: | : ||: | | || : :| |  
Db 193 DQFHGTEYVCCPQT\_KTVDSSTMSKEEEEEEE-----DEEDEEDYDLKSEFPTE 243  
  
Qy 232 EEVAEVEEEEEAD-DEDEDGDEVEEEAE-----EPYEEATERTTSIATTTTTTTTES 282  
: : | || :||:|:|:| | : : : | | | | : : | : :  
Db 244 ADLEDFTAAADEEEEEDEEGEEVVEDRDYYYDPFKGDDYNE--ENPTESPSEGTISDKE 301  
  
Qy 283 VEEVVRVPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAE 342

[illegible]

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RESULT 11
APP2_HUMAN
ID APP2_HUMAN STANDARD; PRT; 763 AA.
AC Q06481;
DT 01-JUN-1994 (Rel. 29, Created)
DT 01-OCT-1996 (Rel. 34, Last sequence update)
DT 15-MAR-2004 (Rel. 43, Last annotation update)
DE Amyloid-like protein 2 precursor (Amyloid protein homolog) (APPH)
DE (CDEI-box binding protein) (CDEBP).
GN APLP2 OR APPL2.
OS Homo sapiens (Human).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
OX NCBI_TaxID=9606;
RN [1]
RP SEQUENCE FROM N.A.
RC TISSUE=Placenta;
RX MEDLINE=93250009; PubMed=8485127;
RA Sprecher C.A., Grant F.J., Grimm G., O'Hara P.J., Norris F.,
RA Norris K., Foster D.C.;
RT "Molecular cloning of the cDNA for a human amyloid precursor protein
RT homolog: evidence for a multigene family.";
RL Biochemistry 32:4481-4486(1993).
RN [2]
RP SEQUENCE FROM N.A.

```

RC TISSUE=Ovary;  
 RX MEDLINE=95217334; PubMed=7702756;  
 RA von der Kammer H., Hanes J., Klaudiny J., Scheit K.H.;  
 RT "A human amyloid precursor-like protein is highly homologous to a  
 RT mouse sequence-specific DNA-binding protein.";  
 RL DNA Cell Biol. 13:1137-1143(1994).  
 RN [3]  
 RP SEQUENCE FROM N.A.  
 RC TISSUE=Brain;  
 RX MEDLINE=94035131; PubMed=8220435;  
 RA Wasco W., Gurubhagavatula S., Paradis M., Romano D.M., Sisodia S.S.,  
 RA Hyman B.T., Neve R.L., Tanzi R.E.;  
 RT "Isolation and characterization of APLP2 encoding a homologue of the  
 RT Alzheimer's associated amyloid beta protein precursor.";  
 RL Nat. Genet. 5:95-99(1993).  
 RN [4]  
 RP SEQUENCE FROM N.A. (ISOFORM 3).  
 RC TISSUE=Lung;  
 RX MEDLINE=22388257; PubMed=12477932;  
 RA Strausberg R.L., Feingold E.A., Grouse L.H., Derge J.G.,  
 RA Klausner R.D., Collins F.S., Wagner L., Shenmen C.M., Schuler G.D.,  
 RA Altschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., Bhat N.K.,  
 RA Hopkins R.F., Jordan H., Moore T., Max S.I., Wang J., Hsieh F.,  
 RA Diatchenko L., Marusina K., Farmer A.A., Rubin G.M., Hong L.,  
 RA Stapleton M., Soares M.B., Bonaldo M.F., Casavant T.L., Scheetz T.E.,  
 RA Brownstein M.J., Usdin T.B., Toshiyuki S., Carninci P., Prange C.,  
 RA Raha S.S., Loquellano N.A., Peters G.J., Abramson R.D., Mullahy S.J.,  
 RA Bosak S.A., McEwan P.J., McKernan K.J., Malek J.A., Gunaratne P.H.,  
 RA Richards S., Worley K.C., Hale S., Garcia A.M., Gay L.J., Hulyk S.W.,  
 RA Villalon D.K., Muzny D.M., Sodergren E.J., Lu X., Gibbs R.A.,  
 RA Fahey J., Helton E., Kettelman M., Madan A., Rodrigues S., Sanchez A.,  
 RA Whiting M., Madan A., Young A.C., Shevchenko Y., Bouffard G.G.,  
 RA Blakesley R.W., Touchman J.W., Green E.D., Dickson M.C.,  
 RA Rodriguez A.C., Grimwood J., Schmutz J., Myers R.M.,  
 RA Butterfield Y.S.N., Krzywinski M.I., Skalska U., Smailus D.E.,  
 RA Schnerch A., Schein J.E., Jones S.J.M., Marra M.A.;  
 RT "Generation and initial analysis of more than 15,000 full-length  
 RT human and mouse cDNA sequences.";  
 RL Proc. Natl. Acad. Sci. U.S.A. 99:16899-16903(2002).  
 CC -!- FUNCTION: May play a role in the regulation of hemostasis. The  
 CC soluble form may have inhibitory properties towards coagulation  
 CC factors. May interact with cellular G-protein signaling pathways.  
 CC May bind to the DNA 5'-GTCACATG-3' (CDEI box).  
 CC -!- SUBCELLULAR LOCATION: Type I membrane protein and nuclear  
 CC (Potential).  
 CC -!- ALTERNATIVE PRODUCTS:  
 CC Event=Alternative splicing; Named isoforms=3;  
 CC Comment=Additional isoforms seem to exist;  
 CC Name=1;  
 CC IsoId=Q06481-1; Sequence=Displayed;  
 CC Name=2;  
 CC IsoId=Q06481-2; Sequence=VSP\_000018;  
 CC Name=3;  
 CC IsoId=Q06481-3; Sequence=VSP\_000019;  
 CC -!- TISSUE SPECIFICITY: In placenta, brain, heart, lung, liver, kidney  
 CC and endothelial tissues.  
 CC -!- SIMILARITY: Belongs to the APP family.

```

CC  -!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.
CC  -----
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CC  -----
DR  EMBL; S60099; AAC60589.1; -.
DR  EMBL; L09209; AAA35526.1; -.
DR  EMBL; Z22572; CAA80295.1; -.
DR  EMBL; L27631; AAC41701.1; -.
DR  EMBL; BC000373; AAH00373.1; -.
DR  PIR; A49321; A49321.
DR  HSSP; P05067; 1MWP.
DR  Genew; HGNC:598; APLP2.
DR  MIM; 104776; -.
DR  GO; GO:0016021; C:integral to membrane; NAS.
DR  GO; GO:0005634; C:nucleus; IDA.
DR  GO; GO:0003677; F:DNA binding; NAS.
DR  GO; GO:0007186; P:G-protein coupled receptor protein signalin. . .; NAS.
DR  InterPro; IPR008155; A4_APP.
DR  InterPro; IPR008154; A4_extra.
DR  InterPro; IPR002223; Kunitz_BPTI.
DR  Pfam; PF02177; A4_EXTRA; 1.
DR  Pfam; PF00014; Kunitz_BPTI; 1.
DR  PRINTS; PR00203; AMYLOIDA4.
DR  PRINTS; PR00759; BASICPTASE.
DR  ProDom; PD000222; Kunitz_BPTI; 1.
DR  SMART; SM00006; A4_EXTRA; 1.
DR  SMART; SM00131; KU; 1.
DR  PROSITE; PS00319; A4_EXTRA; 1.
DR  PROSITE; PS00320; A4_INTRA; 1.
DR  PROSITE; PS00280; BPTI_KUNITZ_1; 1.
DR  PROSITE; PS50279; BPTI_KUNITZ_2; 1.
KW  Transmembrane; Signal; Alternative splicing; DNA-binding;
KW  Nuclear protein; Serine protease inhibitor.
FT  SIGNAL          1      29      POTENTIAL.
FT  CHAIN           30     763     AMYLOID-LIKE PROTEIN 2.
FT  DOMAIN          30     692     EXTRACELLULAR (POTENTIAL).
FT  TRANSMEM        693     716     POTENTIAL.
FT  DOMAIN          717     763     CYTOPLASMIC (POTENTIAL).
FT  DOMAIN          215     280     ASP/GLU-RICH (HIGHLY ACIDIC).
FT  DOMAIN          306     364     BPTI/KUNITZ INHIBITOR.
FT  DOMAIN          215     231     POLY-GLU.
FT  ACT_SITE        320     321     REACTIVE BOND (BY SIMILARITY).
FT  DISULFID        310     360     BY SIMILARITY.
FT  DISULFID        319     343     BY SIMILARITY.
FT  DISULFID        335     356     BY SIMILARITY.
FT  VARSPLIC        308     363     Missing (in isoform 2).
FT                                     /FTId=VSP_000018.
FT  VARSPLIC        613     624     Missing (in isoform 3).
FT                                     /FTId=VSP_000019.
FT  CONFLICT        543     543     S -> I (IN REF. 1).
SQ  SEQUENCE        763 AA;  86955 MW;  CA3A7D6DDB8A28D0 CRC64;

```

Query Match 47.2%; Score 1725; DB 1; Length 763;  
Best Local Similarity 46.9%; Pred. No. 1.6e-77;  
Matches 369; Conservative 112; Mismatches 170; Indels 136; Gaps 19;

```
Qy      5 LALLLLAAWTARALEV-----PTDGNAG---LLAEPQIAMFCGRLNMHMNVQNGKWDSDP 56
      | | | | | | | | | | : | | | | | : | | | | | | | | | | | | | | | | |
Db     15 LLLLLLVGLTAPALALAGYIEALAANAGTGFAVAEPQIAMFCGKLNMHVNIQTGWEPDP 74

Qy     57 SGTKTCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYR 116
      : | | | : | | | : | | | | | | | | | | | | | | | | | | | | | | | |
Db     75 TGTKSCFETKEEVLYCQEMYPELQITNVMEANQRVSIDNWCRRDKKQCKS--RFVTPFK 132

Qy    117 CLVGEFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGI 176
      | | | | | | | | | | : | | | : | | | | | | | | | | | | | | | | |
Db    133 CLVGEFVSDVLLVPEKCQFFHKERMEVCENHQHWHTVVKEACLTQGMTLYSYGMLLPCGV 192

Qy    177 DKFRGVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAE 236
      | : | | | : | | | : | | | : | | | : | | | : | | | : | | |
Db    193 DQFHGTEYVCCPQTKIIGSVSKEEEEEDEE-----EEEEDEEEDYDVYKSEFPTEAD 245

Qy    237 VEE--EEA--DDDEDDEDGDEVEEEAEOPY-----EEATERTTSIATTTTTTTES 282
      : | : | | : | | | : | | | : | | | : | | | : | | | : | | |
Db    246 LEDFTEAAVDEDEDEEEGEEVVEDRDYYYDTFKGDDYNEENPTEPGSDGTMSDKEITHD 305

Qy    283 VEEV-----VRVP 290
      | : | | | | | | | | | | | | | | | | | | | | | | | | | | |
Db    306 VKAVCSQEAMTGPCRAVMPRWYFDLSKGKCVRFIYGCGGNRNNFESEDYCMVCKAMIP 365

Qy    291 TTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPK 350
      | | | | | | | | | | : | | | | | | | | | | : | | | | | | | | | |
Db    366 PTPLPTND-VDVYFETSADDNEHARFQKAKEQLEIRHRNRMDRVKKEWEEAELQAKNLPK 424

Qy    351 ADKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPP 410
      | : : : : | | | | | : : : : | | | | | : : : : | | | | | : | |
Db    425 AERQTLIQHFQAMVKALEKEAASEKQQLVETHLARVEAMLNDRRRMALENYLAALQSDPP 484

Qy    411 RPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSL 470
      | | : | : | | | | | | | | | | | | | | | | | | | | | | | |
Db    485 RPHRILQALRRYVRAENKDRDLHTIRHYQHVLAVDPEKAAQMKSQVMTHLHVIERRNQSL 544

Qy    471 SLLYNVPAVAEEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDAIMPSTETKTVE 530
      | | | | | | | | | | : | | | : | | | : | | | : | | | : | | |
Db    545 SLLYKVPYVAQEIQEEIDELLQEQR-----ADM-----DQFTASISETPVDVR 587

Qy    531 LLPVNGEFSLDDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPG-----SGLTN 585
      | : | | : : | : | | | | | | | | | | | | | | | | | | | |
Db    588 ---VSSEES-EEIPPFHPF--HPFPALPENE----DTQPELYHPMKKSGVGEQDGGGLIG 637

Qy    586 IKTEEISEVN-LDAEFRHDSGYEVHHQKLVFFAEDVGS-----NKGAI 627
      : : | : | : | | | | | : | : : : | | | | | : | :
Db    638 AEEKVINSKNKV DENMVIDETLDV--KEMIFNAERVGGLEEEERESVGPLREDFSLSSAL 695

Qy    628 IGLMVGGVVIATVIVITLVMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTY 687
      | | | : | | | | | | | | | | : | | | | | | | | | | : | | | |
Db    696 IGLLVIAVAIATVIVISLVMLRKRQYGTISHGIVEVDPMLTPEERHLNKMQNHYENPTY 755
```

Qy            688 KFFEQQ 694  
             |: ||||  
Db            756 KYLEQQ 762

RESULT 12

APP2\_RAT

ID    APP2\_RAT            STANDARD;            PRT;    765 AA.  
AC    P15943;  
DT    01-APR-1990 (Rel. 14, Created)  
DT    01-OCT-1996 (Rel. 34, Last sequence update)  
DT    28-FEB-2003 (Rel. 41, Last annotation update)  
DE    Amyloid-like protein 2 precursor (Sperm membrane protein YWK-II).  
GN    APLP2.  
OS    Rattus norvegicus (Rat).  
OC    Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
OC    Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Rattus.  
OX    NCBI\_TaxID=10116;  
RN    [1]  
RP    SEQUENCE OF 1-627 FROM N.A.  
RC    STRAIN=Wistar; TISSUE=Brain, and Heart;  
RX    MEDLINE=94368849; PubMed=8086458;  
RA    Sandbrink R., Masters C.L., Beyreuther K.;  
RT    "Complete nucleotide and deduced amino acid sequence of rat amyloid  
RT    protein precursor-like protein 2 (APLP2/APPH): two amino acids length  
RT    difference to human and murine homologues.";  
RL    Biochim. Biophys. Acta 1219:167-170(1994).  
RN    [2]  
RP    SEQUENCE OF 575-765 FROM N.A.  
RC    TISSUE=Testis;  
RX    MEDLINE=90207205; PubMed=1690887;  
RA    Yan Y.C., Bai Y., Wang L.F., Miao S.Y., Koide S.S.;  
RT    "Characterization of cDNA encoding a human sperm membrane protein  
RT    related to A4 amyloid protein.";  
RL    Proc. Natl. Acad. Sci. U.S.A. 87:2405-2408(1990).  
CC    -!- SUBCELLULAR LOCATION: Type I membrane protein.  
CC    -!- ALTERNATIVE PRODUCTS:  
CC        Event=Alternative splicing; Named isoforms=4;  
CC        Name=A;  
CC        IsoId=P15943-1; Sequence=Displayed;  
CC        Name=B;  
CC        IsoId=P15943-2; Sequence=VSP\_000021;  
CC        Name=C;  
CC        IsoId=P15943-3; Sequence=VSP\_000020;  
CC        Name=D;  
CC        IsoId=P15943-4; Sequence=VSP\_000020, VSP\_000021;  
CC    -!- SIMILARITY: Belongs to the APP family.  
CC    -!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.

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CC    -----



DR EMBL; X77934; CAA54906.1; -.  
 DR EMBL; M31322; AAA42352.1; -.  
 DR PIR; A35981; A35981.  
 DR PIR; S42880; S42880.  
 DR HSSP; P05067; 1MWP.  
 DR InterPro; IPR008155; A4\_APP.  
 DR InterPro; IPR008154; A4\_extra.  
 DR InterPro; IPR002223; Kunitz\_BPTI.  
 DR Pfam; PF02177; A4\_EXTRA; 1.  
 DR Pfam; PF00014; Kunitz\_BPTI; 1.  
 DR PRINTS; PR00203; AMYLOIDA4.  
 DR PRINTS; PR00759; BASICPTASE.  
 DR ProDom; PD000222; Kunitz\_BPTI; 1.  
 DR SMART; SM00006; A4\_EXTRA; 1.  
 DR SMART; SM00131; KU; 1.  
 DR PROSITE; PS00319; A4\_EXTRA; 1.  
 DR PROSITE; PS00320; A4\_INTRA; 1.  
 DR PROSITE; PS00280; BPTI\_KUNITZ\_1; 1.  
 DR PROSITE; PS50279; BPTI\_KUNITZ\_2; 1.  
 KW Transmembrane; Alternative splicing; Serine protease inhibitor;  
 KW Signal; Glycoprotein.  
 FT SIGNAL 1 29 POTENTIAL.  
 FT CHAIN 30 765 AMYLOID-LIKE PROTEIN 2.  
 FT DOMAIN 30 695 EXTRACELLULAR (POTENTIAL).  
 FT TRANSMEM 696 718 POTENTIAL.  
 FT DOMAIN 719 765 CYTOPLASMIC (POTENTIAL).  
 FT DOMAIN 218 282 ASP/GLU-RICH (HIGHLY ACIDIC).  
 FT DOMAIN 308 366 BPTI/KUNITZ INHIBITOR.  
 FT ACT\_SITE 322 323 REACTIVE BOND (BY SIMILARITY).  
 FT DISULFID 312 362 BY SIMILARITY.  
 FT DISULFID 321 345 BY SIMILARITY.  
 FT DISULFID 337 358 BY SIMILARITY.  
 FT DOMAIN 218 229 POLY-GLU.  
 FT CARBOHYD 628 628 O-LINKED (GLYCOSAMINOGLYCAN) (POTENTIAL).  
 FT VARSPLIC 311 365 Missing (in isoform C and isoform D).  
 FT /FTId=VSP\_000020.  
 FT VARSPLIC 616 627 Missing (in isoform B and isoform D).  
 FT /FTId=VSP\_000021.  
 FT CONFLICT 575 577 DQF -> EFV (IN REF. 2).  
 SQ SEQUENCE 765 AA; 86882 MW; CF51FCCCE305A0CF CRC64;

Query Match 46.8%; Score 1709; DB 1; Length 765;  
 Best Local Similarity 45.9%; Pred. No. 9.5e-77;  
 Matches 361; Conservative 124; Mismatches 168; Indels 134; Gaps 20;

Qy 5 LALLLLAAWTARALEV-----PTDGNAG---LLAEPQIAMFCGRLNMHMNVQNGKWSDP 56  
 | :||| || | : ||| :|||||||:||||:|:| |||: ||  
 Db 15 LLVLLLLGLTAPAAALAGYIEALANAGTGFAVAEPQIAMFCGKLNHVNITGKWEPPD 74  
 Qy 57 SGTKTCTIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYR 116  
 :|||:|: ||| :|||||:|||||||:||||| | :||:| :|||:| | |||:|  
 Db 75 TGTKSCLGTKEEVLQYCQEIYPELQITNVMEANQPVNIDSWCRRDKKQCRS--HIVIPFK 132  
 Qy 117 CLVGEFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGI 176  
 ||||| ||||: |:| ||||:||| | |||| || | : |: |||||:|  
 Db 133 CLVGEFVSDVLLVPENCQFFHQERMEVCEKHQRWHTVVKEACLTEGMTLYSYGMLLPCGV 192

Qy	177	DKFRGVFVCCPLAE--ESDNVDSADAEEDSDVWVGADTDYA-DGSEDKVVEVAEEEE	233
Db	193	DQFHGTEYVCCPQTKVVDSDSTMSKEEEEEEEEE-----DEEEDYALDKSEFPTEADLEDFT	248
Qy	234	VAVEVEEEEADDDDEDDGDEVEEEAEOPYEE-----ATERTTSIATTTTTTTESVEEVV	287
Db	249	EAAADEDEDEEEEEEEEEEGEEVVEDRDYYYDSFKGDDYNEENPTEPSSDGTISDKEDIAHDV	308
Qy	288	R-----VPT	291
Db	309	KAVCSQEAMTGPCRAVMPRWYFDLSKGKCVRFIYGGCGGNRRNFESEDYCMVCKTMI PP	368
Qy	292	TAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKA	351
Db	369	TPLPTND-VDVYFETSADDNEHARFQKAKEQLEIRHRSRMDRVKKEWEEAELQAKNLPKA	427
Qy	352	DKKAVIQHFQEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPR	411
Db	428	ERQTLIQHFQAMVKALEKEAASEKQQLVETHLARVEAMLNDRRLALENYLAALQSDPPR	487
Qy	412	PRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSL	471
Db	488	PHRILQALRRYVRAENKDRLHTIRHYQHVLAVDPEKAAQMKSQVMTHLVIEERNQSL	547
Qy	472	LLYNVPAVAEEIQDEVDELLQKEQNYSDDLANMISEPRISYGNDALMPSLTETKTTVEL	531
Db	548	LLYKVPYVAQEIQEEIDELLQEQR-----ADM-----DQFTSSISENPVDVR-	589
Qy	532	LPVNGEFLDDLQPWHSFGADSVPAANTENEVEPVDARP-----AADRGLTTRPGSGLTN	585
Db	590	--VSSEES-EEIPPFHPF--HPFPLSENE----DTQPELYHPMKKGSGMAEQDG-GLIG	639
Qy	586	IKTEEISEVN-LDAEFRHDSGYEVHHQKLVFFFAEDVGS-----NKGAI	627
Db	640	AEEKVINSKNKMDENMVIDETLDV--KEMIFNAERVGGLEEEPDVSGPLREDFSLSSSAL	697
Qy	628	IGLMVGGVVIATVIVITLVLMLKKQYTSIHHGVVEVDAAVTPEERHLSKMQQNGYENPTY	687
Db	698	IGLLVIAVAIATVIVISLVLMLRKROYGTISHGIVEVHPMLTPEERHLNKMQNHYENPTY	757
Qy	688	KFFEQMQ 694	
Db	758	KYLEQMQ 764	

RESULT 13

ID APP1 HUMAN STANDARD; PRT; 650 AA.

AC P51693; 000113; Q96A92;

DT 28-FEB-2003 (Rel. 41, Last sequence update)

DT 15-MAR-2004 (Rel. 43, Last annotation update)

DE Amyloid-like protein 1 precursor (APLP) (APLP-1) [Contains: C30].

GN APLP1.

OS Homo sapiens (Human).

OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;

OC Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.

OX NCBI\_TaxID=9606;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RX MEDLINE=98088960; PubMed=9428684;  
 RA Paliga K., Peraus G., Kreger S., Duwrrwang U., Hesse L., Multhaup G.,  
 RA Masters C.L., Beyreuther K., Weidemann A.;  
 RT "Human amyloid precursor-like protein 1 -- cDNA cloning, ectopic  
 RT expression in COS-7 cells and identification of soluble forms in the  
 RT cerebrospinal fluid.";  
 RL Eur. J. Biochem. 250:354-363(1997).  
 RN [2]  
 RP SEQUENCE FROM N.A.  
 RX MEDLINE=98180887; PubMed=9521588;  
 RA Lenkkeri U., Kestila M., Lamerdin J., McCready P., Adamson A.,  
 RA Olsen A., Tryggvason K.;  
 RT "Structure of the human amyloid-precursor-like protein gene APLP1 at  
 RT 19q13.1.";  
 RL Hum. Genet. 102:192-196(1998).  
 RN [3]  
 RP SEQUENCE FROM N.A.  
 RC TISSUE=Ovary;  
 RX MEDLINE=22388257; PubMed=12477932;  
 RA Strausberg R.L., Feingold E.A., Grouse L.H., Derge J.G.,  
 RA Klausner R.D., Collins F.S., Wagner L., Shenmen C.M., Schuler G.D.,  
 RA Altschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., Bhat N.K.,  
 RA Hopkins R.F., Jordan H., Moore T., Max S.I., Wang J., Hsieh F.,  
 RA Diatchenko L., Marusina K., Farmer A.A., Rubin G.M., Hong L.,  
 RA Stapleton M., Soares M.B., Bonaldo M.F., Casavant T.L., Scheetz T.E.,  
 RA Brownstein M.J., Usdin T.B., Toshiyuki S., Carninci P., Prange C.,  
 RA Raha S.S., Loquellano N.A., Peters G.J., Abramson R.D., Mullahy S.J.,  
 RA Bosak S.A., McEwan P.J., McKernan K.J., Malek J.A., Gunaratne P.H.,  
 RA Richards S., Worley K.C., Hale S., Garcia A.M., Gay L.J., Hulyk S.W.,  
 RA Villalon D.K., Muzny D.M., Sodergren E.J., Lu X., Gibbs R.A.,  
 RA Fahey J., Helton E., Kettelman M., Madan A., Rodrigues S., Sanchez A.,  
 RA Whiting M., Madan A., Young A.C., Shevchenko Y., Bouffard G.G.,  
 RA Blakesley R.W., Touchman J.W., Green E.D., Dickson M.C.,  
 RA Rodriguez A.C., Grimwood J., Schmutz J., Myers R.M.,  
 RA Butterfield Y.S.N., Krzywinski M.I., Skalska U., Smailus D.E.,  
 RA Schnerch A., Schein J.E., Jones S.J.M., Marra M.A.;  
 RT "Generation and initial analysis of more than 15,000 full-length  
 RT human and mouse cDNA sequences.";  
 RL Proc. Natl. Acad. Sci. U.S.A. 99:16899-16903(2002).  
 RN [4]  
 RP POSSIBLE FUNCTION, AND TISSUE SPECIFICITY.  
 RX MEDLINE=96115107; PubMed=7494461;  
 RA Kim T.-W., Wu K., Xu J.-L., McAuliffe G., Tanzi R.E., Wasco W.,  
 RA Black I.B.;  
 RT "Selective localization of amyloid precursor-like protein 1 in the  
 RT cerebral cortex postsynaptic density.";  
 RL Brain Res. Mol. Brain Res. 32:36-44(1995).  
 RN [5]  
 RP HEPARIN AND ZINC BINDING.  
 RX MEDLINE=95014513; PubMed=7929392;  
 RA Bush A.I., Pettingell W.H. Jr., de Paradis M., Tanzi R.E., Wasco W.;  
 RT "The amyloid beta-protein precursor and its mammalian homologues.  
 RT Evidence for a zinc-modulated heparin-binding superfamily.";  
 RL J. Biol. Chem. 269:26618-26621(1994).

RN [6]  
RP INTERACTION WITH APBA2.  
RX MEDLINE=99107877; PubMed=9890987;  
RA Tomita S., Ozaki T., Taru H., Oguchi S., Takeda S., Yagi Y.,  
RA Sakiyama S., Kirino Y., Suzuki T.;  
RT "Interaction of a neuron-specific protein containing PDZ domains with  
RT Alzheimer's amyloid precursor protein.";  
RL J. Biol. Chem. 274:2243-2254(1999).

RN [7]  
RP EXTRACELLULAR COPPER-BINDING.  
RX MEDLINE=22130992; PubMed=12135352;  
RA Simons A., Ruppert T., Schmidt C., Schlicksupp A., Pipkorn R.,  
RA Reed J., Masters C.L., White A.R., Cappai R., Beyreuther K.,  
RA Bayer T.A., Multhaup G.;  
RT "Evidence for a copper-binding superfamily of the amyloid precursor  
RT protein.";  
RL Biochemistry 41:9310-9320(2000).  
CC -!- FUNCTION: May play a role in postsynaptic function. The C-terminal  
CC gamma-secretase processed fragment, ALID1, activates transcription  
CC activation through APBB1 (Fe65) binding (By similarity). Couples  
CC to JIP signal transduction through C-terminal binding. May  
CC interact with cellular G-protein signaling pathways. Can regulate  
CC neurite outgrowth through binding to components of the  
CC extracellular matrix such as heparin and collagen I.  
CC -!- FUNCTION: The gamma-CTF peptide, C30, is a potent enhancer of  
CC neuronal apoptosis (By similarity).  
CC -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several  
CC cytoplasmic proteins, including APBB and APBA family members,  
CC MAPK8IP1 and Dab1 (By similarity). Binding to Dab1 inhibits its  
CC serine phosphorylation (By similarity).  
CC -!- SUBCELLULAR LOCATION: Type I membrane protein. C-terminally  
CC processed in the Golgi complex.  
CC -!- TISSUE SPECIFICITY: Expressed in the cerebral cortex where it is  
CC localized to the postsynaptic density (PSD).  
CC -!- DOMAIN: The NPXY sequence motif found in many tyrosine-  
CC phosphorylated proteins is required for the specific binding of  
CC the PID domain. However additional amino acids either N- or C-  
CC terminal to the NPXY motif are often required for complete  
CC interaction. The NPXY site is also involved in clathrin-mediated  
CC endocytosis.  
CC -!- PTM: Proteolytically cleaved by caspases during neuronal  
CC apoptosis. Cleaved, in vitro, at Asp-620 by caspase-3 (By  
CC similarity).  
CC -!- PTM: N- and O-glycosylated.  
CC -!- MISCELLANEOUS: Binds zinc and copper in the extracellular domain.  
CC Zinc-binding increases heparin binding. No Cu(II) reducing  
CC activity with copper-binding.  
CC -!- SIMILARITY: Belongs to the APP family.

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CC or send an email to [license@isb-sib.ch](mailto:license@isb-sib.ch)).  
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Qy 120 GEFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKF 179  
 ||||:||||: |:|||||| ||: | |:| || : || ||||| |:|  
 Db 143 GEFVSEALLVPEGCRFLHQERMDQCESSTRRHQEAQEACSSQGLILHGSMLLPCGSDRF 202

Qy 180 RGVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEE 239  
 ||||:|||| | | | | | | | | | | | | | | | | | | | | | |  
 Db 203 RGVEYVCCPPPGLTPD--PSGTAVGDPSTRSW-----PPGSR---VEGADEEE---EE 246

Qy 240 EEADDDDEDD--EDGDEVEEEAEPEYEEATERTTSIATTTTTTTTESVEEVVRVPTTAASTP 297  
 | | | | : : ||| | | : | : | | | | | | | | | | | | | | | |  
 Db 247 ESFPQPVDDYFVEPPQAEEE-EETVPPSSHTLAVVGKVTPTPR-----PT----- 291

Qy 298 DAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVI 357  
 | | | | | | : || | : || | | : : : |||| | | : | | | | | | : : | |  
 Db 292 DGVDIYFGMPGEISEHEGFLRAKMDLEERRMRQINEVMREWAMADNQSKNLPKADRQALN 351

Qy 358 QHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFN 417  
 : || | : : || : : | ||:|||| | | | : ||: || | | | : || | | | |  
 Db 352 EHFQSILQTLQEEQVSGERQRLVETHATRVIALINDQRRAALEGFLAALQADPPQAERVLL 411

Qy 418 MLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVP 477  
 | : : | : |||| : : || : || | | | | | | | | | | | | | | | | |  
 Db 412 ALRRYLRAEQKEQRHTLRHYQHVAVDPEKAQQMRQVHTHLQVIEERVNQSLGLLDQNP 471

Qy 478 AVAEEIQDEVDELLQKEQNYSDDVLANMISEPRISYGN DALMPSLTETKTTVELLPVNGE 537  
 : | : : : : || | | | | | | | | | | | | | | | | | | | | | |  
 Db 472 HLAQELRPQIQELLHSEH-----LGPSELEA-----PAPGG 502

Qy 538 FSLDDLQPWHSFGADSVPA NTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD 597  
 | | | | : : | | : | | | | | : : | | : : | | : : | |  
 Db 503 SSED-----KGGLQPPDSKD--DTPMTLPKGSTEQDAASPEKEKMNPL 543

Qy 598 AEF RH-----DSGYEVH---QKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVM 648  
 : : | : | | : | : | : | : | : | : | : | : | : | : | : | : |  
 Db 544 EQYERKVNASVPRGFPHSSEIQRDELAPAGTGV SREAVSGLLIMGAGGSLIVLSMLLL 603

Qy 649 -KKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQ 692  
 : || | : | | |||| | : | | : | : | : | : | : | : | : | : | : |  
 Db 604 RRKKPYGAISHGVVEVDPMLTLEEQLRELQRHGYENPTYRFL 648

# RESULT 14

## APPL\_MOUSE

ID APPL\_MOUSE STANDARD; PRT; 653 AA.  
 AC Q03157; Q8VC38;  
 DT 01-OCT-1993 (Rel. 27, Created)  
 DT 01-OCT-1993 (Rel. 27, Last sequence update)  
 DT 15-MAR-2004 (Rel. 43, Last annotation update)  
 DE Amyloid-like protein 1 precursor (APLP) (APLP-1) [Contains: C30].  
 GN APLP1.  
 OS Mus musculus (Mouse).  
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
 OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.  
 OX NCBI\_TaxID=10090;  
 RN [1]  
 RP SEQUENCE FROM N.A.

RC TISSUE=Brain;  
 RX MEDLINE=93066322; PubMed=1279693;  
 RA Wasco W., Bupp K., Magendantz M., Gusella J.F., Tanzi R.E.,  
 RA Solomon F.;  
 RT "Identification of a mouse brain cDNA that encodes a protein related  
 RT to the Alzheimer disease-associated amyloid beta protein precursor.";  
 RL Proc. Natl. Acad. Sci. U.S.A. 89:10758-10762(1992).  
 RN [2]  
 RP SEQUENCE FROM N.A.  
 RC TISSUE=Retina;  
 RX MEDLINE=22388257; PubMed=12477932;  
 RA Strausberg R.L., Feingold E.A., Grouse L.H., Derge J.G.,  
 RA Klausner R.D., Collins F.S., Wagner L., Shenmen C.M., Schuler G.D.,  
 RA Altschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., Bhat N.K.,  
 RA Hopkins R.F., Jordan H., Moore T., Max S.I., Wang J., Hsieh F.,  
 RA Diatchenko L., Marusina K., Farmer A.A., Rubin G.M., Hong L.,  
 RA Stapleton M., Soares M.B., Bonaldo M.F., Casavant T.L., Scheetz T.E.,  
 RA Brownstein M.J., Usdin T.B., Toshiyuki S., Carninci P., Prange C.,  
 RA Raha S.S., Loquellano N.A., Peters G.J., Abramson R.D., Mullahy S.J.,  
 RA Bosak S.A., McEwan P.J., McKernan K.J., Malek J.A., Gunaratne P.H.,  
 RA Richards S., Worley K.C., Hale S., Garcia A.M., Gay L.J., Hulyk S.W.,  
 RA Villalon D.K., Muzny D.M., Sodergren E.J., Lu X., Gibbs R.A.,  
 RA Fahey J., Helton E., Kettelman M., Madan A., Rodrigues S., Sanchez A.,  
 RA Whiting M., Madan A., Young A.C., Shevchenko Y., Bouffard G.G.,  
 RA Blakesley R.W., Touchman J.W., Green E.D., Dickson M.C.,  
 RA Rodriguez A.C., Grimwood J., Schmutz J., Myers R.M.,  
 RA Butterfield Y.S.N., Krzywinski M.I., Skalska U., Smailus D.E.,  
 RA Schnerch A., Schein J.E., Jones S.J.M., Marra M.A.;  
 RT "Generation and initial analysis of more than 15,000 full-length  
 RT human and mouse cDNA sequences.";  
 RL Proc. Natl. Acad. Sci. U.S.A. 99:16899-16903(2002).  
 RN [3]  
 RP COLLAGEN-BINDING.  
 RX MEDLINE=96139497; PubMed=8576160;  
 RA Beher D., Hesse L., Masters C.L., Multhaup G.;  
 RT "Regulation of amyloid protein precursor (APP) binding to collagen and  
 RT mapping of the binding sites on APP and collagen type I.";  
 RL J. Biol. Chem. 271:1613-1620(1996).  
 RN [4]  
 RP INTERACTION WITH DAB1.  
 RX MEDLINE=99389880; PubMed=10460257;  
 RA Homayouni R., Rice D.S., Sheldon M., Curran T.;  
 RT "Disabled-1 binds to the cytoplasmic domain of amyloid precursor-like  
 RT protein 1.";  
 RL J. Neurosci. 19:7507-7515(1999).  
 RN [5]  
 RP INTERACTION WITH MAPK8IP1.  
 RX MEDLINE=21408156; PubMed=11517249;  
 RA Matsuda S., Yasukawa T., Homma Y., Ito Y., Niikura T., Hiraki T.,  
 RA Hirai S., Ohno S., Kita Y., Kawasumi M., Kouyama K., Yamamoto T.,  
 RA Kyriakis J.M., Nishimoto I.;  
 RT "C-jun N-terminal kinase (JNK)-interacting protein-1b/islet-brain-1  
 RT scaffolds Alzheimer's amyloid precursor protein with JNK.";  
 RL J. Neurosci. 21:6597-6607(2001).  
 RN [6]  
 RP GAMMA-SECRETASE PROCESSING, INTERACTION WITH APBB1, AND MUTAGENESIS OF  
 RP TYR-641.

RX MEDLINE=22313598; PubMed=12228233;  
 RA Scheinfeld M.H., Ghersi E., Laky K., Fowlkes B.J., D'Adamio L.;  
 RT "Processing of beta-amyloid precursor-like protein-1 and -2 by gamma-  
 RT secretase regulates transcription.";  
 RL J. Biol. Chem. 277:44195-44201(2002).  
 CC -!- FUNCTION: May play a role in postsynaptic function. The C-terminal  
 CC gamma-secretase processed fragment, ALID1, activates transcription  
 CC activation through APBB1 (Fe65) binding. Couples to JIP signal  
 CC transduction through C-terminal binding. May interact with  
 CC cellular G-protein signaling pathways. Can regulate neurite  
 CC outgrowth through binding to components of the extracellular  
 CC matrix such as heparin and collagen I.  
 CC -!- FUNCTION: The gamma-CTF peptide, C30, is a potent enhancer of  
 CC neuronal apoptosis (By similarity).  
 CC -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several  
 CC cytoplasmic proteins, including APBB and APBA family members,  
 CC MAPK8IP1 and Dab1 (By similarity). Binding to Dab1 inhibits its  
 CC serine phosphorylation.  
 CC -!- SUBCELLULAR LOCATION: Type I membrane protein. C-terminally  
 CC processed in the Golgi complex.  
 CC -!- DOMAIN: The NPXY sequence motif found in many tyrosine-  
 CC phosphorylated proteins is required for the specific binding of  
 CC the PID domain. However additional amino acids either N- or C-  
 CC terminal to the NPXY motif are often required for complete  
 CC interaction. The NPXY site is also involved in clathrin-mediated  
 CC endocytosis.  
 CC -!- PTM: Proteolytically cleaved by caspases during neuronal  
 CC apoptosis. Cleaved, in vitro, at Asp-623 by caspase-3 (By  
 CC similarity).  
 CC -!- PTM: N- and O-glycosylated.  
 CC -!- MISCELLANEOUS: Binds zinc and copper in the extracellular domain.  
 CC Zinc-binding increases heparin binding. No Cu(II) reducing  
 CC activity with copper-binding.  
 CC -!- SIMILARITY: Belongs to the APP family.  
 CC -----  
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 CC -----  
 DR EMBL; L04538; AAA37247.1; -.  
 DR EMBL; BC021877; AAH21877.1; -.  
 DR PIR; A46362; A46362.  
 DR HSSP; P05067; 1MWP.  
 DR MGD; MGI:88046; Aplp1.  
 DR InterPro; IPR008155; A4\_APP.  
 DR InterPro; IPR008154; A4\_extra.  
 DR Pfam; PF02177; A4\_EXTRA; 1.  
 DR PRINTS; PR00203; AMYLOIDA4.  
 DR SMART; SM00006; A4\_EXTRA; 1.  
 DR PROSITE; PS00319; A4\_EXTRA; 1.  
 DR PROSITE; PS00320; A4\_INTRA; 1.  
 KW Apoptosis; Endocytosis; Cell adhesion; Coated pits; Neurone;  
 KW Heparin-binding; Metal-binding; Copper; Zinc; Signal; Transmembrane;



KW	Glycoprotein.			
FT	SIGNAL	1	37	POTENTIAL.
FT	CHAIN	38	653	AMYLOID-LIKE PROTEIN 1.
FT	CHAIN	624	653	C30 (BY SIMILARITY).
FT	DOMAIN	38	583	EXTRACELLULAR (POTENTIAL).
FT	TRANSMEM	584	606	POTENTIAL.
FT	DOMAIN	607	653	CYTOPLASMIC (POTENTIAL).
FT	DOMAIN	157	177	COPPER-BINDING.
FT	DOMAIN	203	210	ZINC-BINDING (BY SIMILARITY).
FT	DOMAIN	313	345	HEPARIN-BINDING (BY SIMILARITY).
FT	DOMAIN	413	444	HEPARIN-BINDING (BY SIMILARITY).
FT	DOMAIN	445	462	COLLAGEN-BINDING (BY SIMILARITY).
FT	DOMAIN	263	271	POLY-GLU.
FT	DOMAIN	535	538	POLY-SER.
FT	DOMAIN	601	606	POLY-LEU.
FT	SITE	166	166	REQUIRED FOR COPPER(II) REDUCTION (BY
FT				SIMILARITY).
FT	SITE	607	618	BASOLATERAL SORTING SIGNAL (BY
FT				SIMILARITY).
FT	SITE	623	624	CLEAVAGE (BY CASPASE-3) (BY SIMILARITY).
FT	SITE	641	644	ENDOCYTOSIS SIGNAL.
FT	SITE	643	646	NPXY MOTIF.
FT	CARBOHYD	464	464	N-LINKED (GLCNAC. . .) (POTENTIAL).
FT	CARBOHYD	554	554	N-LINKED (GLCNAC. . .) (POTENTIAL).
FT	MUTAGEN	641	641	Y->G: REDUCED BINDING OF APBB1.
FT	CONFLICT	17	17	P -> PP (IN REF. 2).
SQ	SEQUENCE	653 AA; 72750 MW; 56516DC3EA40E4B0 CRC64;		

Query Match 32.4%; Score 1183; DB 1; Length 653;  
 Best Local Similarity 39.0%; Pred. No. 4.4e-51;  
 Matches 275; Conservative 121; Mismatches 221; Indels 88; Gaps 20;

Qy	1	MLPGLALLLLAAWTARA-LEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPST	59
		:   :              :	
Db	22	LLP-LSLLLLRAQLAVGNLAVGSPSAEAPGSAQVAGLCGRLTLHRDLRTGRWEPDPQRS	80
Qy	60	KTCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHF-VIPYRCL	118
		:   : :   :   :   :	
Db	81	RRCLLDPQRVLEYCRQMPYELHARVEQAAQAI PMERWCGGTRSGRCAHPHHEVVFFHCL	140
Qy	119	VGEFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDK	178
		:     :   :	
Db	141	PGEFVSEALLVPEGCRFLHQERMDQCESSTRHQEAQAEACSSQGLILHSGMLLPCGSDR	200
Qy	179	FRGVEFVCCPLAEESDNVDSADAEEDSDVW-WGGADTDYADGSEDKVVEVAEEEEVAEV	237
		:      :     : :	
Db	201	FRGVEYVCCP-PPATPNPSGMAAGDPSTRSWPLGGR----AEGGED-----EEEVESF	248
Qy	238	EEEEADDDDEDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTTESVEEVVRVPTTAASTP	297
		:   : :           :   : :	
Db	249	PQPVDYDFVEPPQAESEEEEEERAPPPSSHTPVMVSRVTPTPR-----PT-----	294
Qy	298	DAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVI	357
		:       :       : : :           :   :         :	
Db	295	DGVDVYFGMPGEIGEHEGFLRAKMDLEERRMRQINEVMREWAMADSQSKNLPKADRQALN	354
Qy	358	QHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFN	417

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      :|||  ::||:: : |||:|||| || |:|:| ||| :: |||  ||:  |
Db      355 EHFQSIQTLEEQVSGERQRLVETHATRVIALINDQRRAALEGFLAALQGDPQAERVLM 414
Qy      418 MLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVP 477
      |:|:|:|:|:|:|:|:|:|:|  ||:| | | | | | | | | | | |
Db      415 ALRRYLRAEQKEQRHTLRHYQHVAVDPEKAQQMRFOVQTHLQVIEERMNQSGLLDQNP 474
Qy      478 AVAEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDALMP-SLTETKTTVELLPVNG 536
      :|:|:|:|:|  |||  || :  :  || :| | :| |
Db      475 HLAQELRPQIQELL-----LAEHLGPSEL----DASVPGSSSEDK----- 510
Qy      537 EFSLDDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSG-----LTNIKTEEI 591
      |||  ||: |:|  |  :| | : |  || :: |
Db      511 ----GSLQP-----PESKDDPPVTLP---KGSTDQESSSSGREKLTPLQYE- 550
Qy      592 SEVNLD AEFRHDSGYEVHH---QKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVML 648
      :|| |  |: |  |:  | :: |: |:|:|  :|:|:|:|:|
Db      551 QKVNASA----PRGF PFHSSDIQRDELAPSGTGVSREALSGLLIMGAGGGS LIVLSLLLL 606
Qy      649 -KKKQYTSIH HGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQ 692
      ||| | :| | | | | | | :| ||: | :|:|:| | | | :|
Db      607 RKKKPYGTISHGVVEVD PMLTLEEQLRELQRHGYENPTYRFLEE 651

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# RESULT 15

## A4\_CAEEL

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ID      A4_CAEEL          STANDARD;          PRT;    686 AA.
AC      Q10651; Q18583; Q95ZX1;
DT      28-FEB-2003 (Rel. 41, Created)
DT      28-FEB-2003 (Rel. 41, Last sequence update)
DT      28-FEB-2003 (Rel. 41, Last annotation update)
DE      Beta-amyloid-like protein precursor.
GN      APL-1 OR C42D8.8.
OS      Caenorhabditis elegans.
OC      Eukaryota; Metazoa; Nematoda; Chromadorea; Rhabditida; Rhabditoidea;
OC      Rhabditidae; Peloderinae; Caenorhabditis.
OX      NCBI_TaxID=6239;
RN      [1]
RP      SEQUENCE OF 6-686 FROM N.A.
RC      STRAIN=Bristol N2;
RX      MEDLINE=94089766; PubMed=8265668;
RA      Daigle I., Li C.;
RT      "apl-1, a Caenorhabditis elegans gene encoding a protein related to
RT      the human beta-amyloid protein precursor.";
RL      Proc. Natl. Acad. Sci. U.S.A. 90:12045-12049(1993).
RN      [2]
RP      SEQUENCE FROM N.A.
RC      STRAIN=Bristol N2;
RA      Hallsworth K.;
RL      Submitted (MAY-1996) to the EMBL/GenBank/DDBJ databases.
RN      [3]
RP      REVISIONS, AND ALTERNATIVE SPLICING.
RA      Waterston R.;
RL      Submitted (JUN-2001) to the EMBL/GenBank/DDBJ databases.
CC      -!- SUBCELLULAR LOCATION: Type I membrane protein (Potential).
CC      -!- ALTERNATIVE PRODUCTS:
CC          Event=Alternative splicing; Named isoforms=2;

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CC      Name=a;
CC      IsoId=Q10651-1; Sequence=Displayed;
CC      Name=b;
CC      IsoId=Q10651-2; Sequence=VSP_000017;
CC      Note=No experimental confirmation available;
CC      -!- SIMILARITY: Belongs to the APP family.
CC      -----
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CC      -----
DR      EMBL; U00240; AAC46470.1; ALT_INIT.
DR      EMBL; U56966; AAA98722.1; -.
DR      EMBL; U56966; AAK68242.1; -.
DR      PIR; T15795; T15795.
DR      HSSP; P05067; 1MWP.
DR      WormPep; C42D8.8a; CE04209.
DR      WormPep; C42D8.8b; CE27845.
DR      InterPro; IPR008155; A4_APP.
DR      InterPro; IPR008154; A4_extra.
DR      Pfam; PF02177; A4_EXTRA; 1.
DR      PRINTS; PR00203; AMYLOIDA4.
DR      SMART; SM00006; A4_EXTRA; 1.
DR      PROSITE; PS00319; A4_EXTRA; 1.
KW      Signal; Transmembrane; Amyloid; Neurogenesis; Glycoprotein;
KW      Alternative splicing.
FT      SIGNAL      1      21      POTENTIAL.
FT      CHAIN      22      686      BETA-AMYLOID-LIKE PROTEIN.
FT      DOMAIN      22      621      EXTRACELLULAR (POTENTIAL).
FT      TRANSMEM      622      642      POTENTIAL.
FT      DOMAIN      643      686      CYTOPLASMIC (POTENTIAL).
FT      DOMAIN      205      228      ASP-RICH.
FT      DOMAIN      676      679      CLATHRIN-BINDING (POTENTIAL).
FT      CARBOHYD      84      84      N-LINKED (GLCNAC. . .) (POTENTIAL).
FT      CARBOHYD      201      201      N-LINKED (GLCNAC. . .) (POTENTIAL).
FT      CARBOHYD      249      249      N-LINKED (GLCNAC. . .) (POTENTIAL).
FT      CARBOHYD      417      417      N-LINKED (GLCNAC. . .) (POTENTIAL).
FT      VARSPLIC      538      539      Missing (in isoform b).
FT      /FTId=VSP_000017.
SQ      SEQUENCE      686 AA; 79434 MW; A0816858FDD48608 CRC64;

Query Match      22.3%; Score 815.5; DB 1; Length 686;
Best Local Similarity 29.1%; Pred. No. 4.6e-33;
Matches 222; Conservative 109; Mismatches 276; Indels 155; Gaps 22;

Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGK 60
      :: || : :| | | | | | | | : | | | : | : | | : |
Db      6 LMIGLLIPILVA-TVYAEGSPAGSKRHEKFIPMVAFSCGYRNQYM-TEEGSWKTDDERYA 63

Qy      61 TCIDTKEGILQYCQEVYPQLQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
      || | ||: ||: : || : |||: || : ||: ||: || | | | | : |
Db      64 TCFSGKLDILKYCRKAYPSMNITNIVEYSHEVSISDWCREEGSPCK-WTHSVRPYHCIDG 122

```

Qy 121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTN-----LHDYGMLLPC 174  
 || :|| || :|| | | : || | : | | : : :|| ||  
 Db 123 EFHSEALQVPHDCQFSHVNSRDQCNDYQHWKDEAGKQCKTKKSKGNKMDIVRSFAVLEPC 182

Qy 175 GIDKFRGVEFVCCPLAEESDNVDSADAEEEDSDVWWGGADTDYADGSEDKVVEVAEEEEV 234  
 :| | ||||| || :| : | ::  
 Db 183 ALDMFTGVEFVCCP----NDQTNKTDVQKTK----- 209

Qy 235 AEVEEEEEADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAA 294  
 |:|| ||||| || :| ||:|| ||  
 Db 210 ---EEDDDDDDEDDAYEDDYSEESDEKDEE----- 236

Qy 295 STPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEA-----ERQAKNLP 349  
 | : | | : ||| |:||: ||: ||||: :||:| | : |:||: |  
 Db 237 -EPSSQDPYFKIANWTNEHDDFKKAEMRMDEKHKRKKVDKVMKEWGDLETRYNEQKAKD-P 294

Qy 350 KADKKAVIQ---HFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITAL- 405  
 | :| | ||: | ||:| |:: | ||:||||:| | :| ||  
 Db 295 KGAEKFKSQMNARFQKTVSSLEEEHKRMRKEIEAVHEERVQAMLNEKKRDATHDYRQALA 354

Qy 406 -QAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYE 464  
 | | | ||:|||| || :| : | ||: | :| ||  
 Db 355 THVNKPNKHSVLQSLKAYIRAEKDRMHTLNRYRHLLKADSKEAAAYKPTVIHRLRYIDL 414

Qy 465 RMNQSLSLLYNVP-----AVA--EEIQDEVDELLQKEQNYSDDLANMISEPRISY 513  
 |:|| :||:| :| || :||:| :| | | :| :|  
 Db 415 RINGTLAMLRDFPDLEKYVRPIAVTYWKDYRDEVSPDISVE----DSELTPIIHDDEFSK 470

Qy 514 GN--DALMPSLT----ETKTTVELLPVNGEFLDDLQPWHSFGADSVPAANT---ENEVEP 564  
 | | :| : :|| | :: :| :| :| :|  
 Db 471 NAKLDVKAPTTTAKPVKETDNAKVLPTASDSEEEADEYYEDEDDEQVKKTPDMKKKVKV 530

Qy 565 VDARP-----AADRGLTTRPGSGLTNIKTEE-----ISEVNLD 598  
 || :| | | | | :||:| | :| :|  
 Db 531 VDIKPKEIKVTIEEEKKAPKLVETSVQTDDEDDDEDSSSSTSSSEDEDEDKNIKELRVDI 590

Qy 599 E-----FRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLK 649  
 | :|| ||: | | : :| :| | :  
 Db 591 EPIIDEPASFYRHD-----KLIQSPEVERSASSFQPYVLASAMFITAICIIAFAIT 642

Qy 650 KKQYTSIHGVEVDAAVTPEERHLSKMQQNGYENPTYKFFE 691  
 : | :|| | ||||: || ||||| ||:  
 Db 643 NARRRRAMRGFIEVD-VYTPEERHVAGMQVNGYENPTYSFDD 683

Search completed: July 26, 2004, 12:44:40  
 Job time : 12 secs